Acute pain management — new challenges

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Abstract
Although almost universal in UK hospitals today, inpatient acute pain services (APS) were uncommon prior to 1990 when a review by the commission on the provision of surgical services demonstrated significant shortfalls in patient care. Established to provide simple analgesic interventions in the postoperative setting, today’s APS faces many new challenges, such as the management of acute neuropathic pain and peri-operative pain control in patients with chronic pain or who are opioid tolerant. The APS has a developing role to educate, to prevent postsurgical chronic pain and to facilitate enhanced recovery after surgery (ERAS) programmes. New ways of utilizing old drugs, and novel regional anaesthetic techniques are helping the modern APS to meet the demands of inpatient pain management.

Keywords
Acute pain service; epidural; gabapentin; ketamine; local anaesthetics; opioids; patient-controlled analgesia; pregabalin

Royal College of Anaesthetists CPD matrix: 1D02, 2E01, 2E02

Acute postoperative pain
The perception of pain varies enormously between individuals. The majority of patients experience significant pain following surgery, but this usually improves during their postoperative stay. However, a proportion may exhibit slow resolution of pain with time. A smaller percentage (~12%) may experience worsening pain as time goes on. Patients experiencing worsening pain after surgery are at risk of delayed discharge from hospital and may go on to develop chronic pain. Pharmacological and non-pharmacological interventions before, during and after surgery may influence pain in the short and long term.

Preoperative interventions
Written patient education material given before surgery has been shown to reduce preoperative anxiety and postoperative analgesia requirements. Pain management programmes delivered prior to surgery have been shown to improve pain and function following hip joint replacement.1

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Learning objectives
After reading this article you should be able to:
- list drugs and techniques used to manage acute post-surgical pain
- outline the concept of chronic post-surgical pain
- describe pain management adjustments needed for opioid-tolerant patients

Simple analgesics, such as paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs), given as a premedication have been shown to improve postoperative pain. More recently, atypical analgesics such as gabapentin and pregabalin have also been shown to reduce postoperative opioid requirements and pain, potentially at the cost of increased sedation and slower anaesthetic recovery.2

Intraoperative analgesia
Intraoperative care can be optimized to minimize postoperative pain, using a combination of analgesic drugs and regional anaesthetic techniques. Local anaesthetic techniques, including continuous infusion devices, and thoracic epidural anaesthesia can improve postoperative pain and reduce the incidence of chronic post-surgical pain (CPSP) following some types of surgery.

Pre-emptive versus preventative analgesia
Pre-emptive analgesia refers to the concept of pain relief administered in anticipation of, or prior to, the surgical incision. Preventive analgesia refers to interventions that have a pain-relieving effect beyond their expected duration of action. There is some evidence that α2β calcium channel ligands (such as gabapentin) and N-methyl-D-aspartate receptor (NMDA-R) antagonists (such as ketamine) may act as preventive analgesics.3

Postoperative care
Standard postoperative care now involves the use of patient-controlled analgesia devices, either with intravenous opioids (PCA) or local anaesthetic/opioid combinations via an epidural catheter (PCEA). Although epidural analgesia is still considered the gold-standard of postoperative pain management for thoraco-abdominal surgery, various regional anaesthetic techniques are becoming more popular. These include single-shot local anaesthetic injections and continuous infiltration via catheters placed in the abdominal wall, paravertebral space, inter-pleural space or wound. Abdominal wall blocks, such as the transversus abdominal plane (TAP) block, provide analgesia for somatic structures, but do not effectively block visceral pain transmitted via the sympathetic nervous system and are therefore frequently supplemented by opioid PCA.

Chronic post-surgical pain
Chronic post-surgical pain (CPSP) is defined by the International Association of Study of Pain (IASP) as pain that persists post-operatively beyond the expected time of healing. This is quoted
as 2 months but many authorities argue that inflammation may still be occurring at this time point, and 3 months is now widely used as a cut-off.

The incidence of CPSP is often quoted as between 10 and 50%, depending upon the type of operation involved. However, the prevalence of significant pain interfering with the individual’s quality of life is in the region of 5–10%. The costs of this ‘silent epidemic’ of CPSP are staggering. About 20% of all patients visiting chronic pain clinics cite surgery as a triggering cause. About $100 billion is spent on chronic pain management in the USA every year. The effect on the individual can be dramatic, not uncommonly resulting in loss of employment and disruption of social and family life as well as predisposing to psychological illness.

Predicting and reducing the risk of CPSP has been the focus of much recent research. Some of the risk factors that have been identified are not easily modifiable such as: female sex, younger age group, pre-existing chronic pain conditions and genotype. Recent prospective studies have revealed some modifiable factors, including: recent musculoskeletal strain (odds-ratio (OR) 2.6), pre-existing pain in the operating field (OR 4.8), other chronic preoperative pain (OR 2.8), severe post-surgical pain (OR 3.22) and co-morbid stress symptoms (OR 3.4). All of these contributed to the risk of CPSP in a mixed group of patients at 6 months postoperatively. The incidence of CPSP increased to 70%–80% in patients with three or more risk factors.

One of the most important risk factors for developing CPSP is severe acute postoperative pain. This finding has major implications for the anaesthetist and APS: firstly it is possible to identify those who are at risk of severe postoperative pain and secondly it is possible to improve their postoperative analgesia and reduce the incidence of CPSP. There are several shared risk factors for severe acute postoperative pain and CPSP, many of which can be identified at the preoperative visit. Evidence-based, procedure-specific guidelines are now starting to be produced to reduce the risk of CPSP.

### The use of atypical analgesics

There are a number of neural pathways involved in nociception. Analgesia can be achieved by influencing pathways other than the opioidergic pathway, using a number of atypical analgesics.

**Ketamine** may act to reduce secondary hyperalgesia after surgery and therefore reduce the risk of transition to CPSP — in this way it is an anti-hyperalgesic rather than analgesic agent. Additional effects of ketamine may include reversal of opioid tolerance and prevention of the phenomenon of opioid-induced hyperalgesia (OIH), whereby rapidly escalated opiate doses precipitate a pro-nociceptive state as opposed to an analgesic effect.

**Clonidine** is an α2-adrenergic agonist that has been used extensively as an analgesic adjunct. Clonidine is thought to act by enhancing activity in descending noradrenergic inhibitory pathways. It has been used in central neuroaxial and regional blocks to prolong analgesia. Systemic administration has less analgesic effect and sedation and hypotension are common side-effects.

**Gabapentin** and **pregabalin** bind competitively to the α2δ subunit of voltage-gated calcium channels in the central nervous system. They have been studied perioperatively with a number of positive effects including reduced anxiety and reduced postoperative opiate requirements. However, the evidence is not clear-cut and some detrimental effects have been reported including sedation and slower post-anaesthetic wake-up. There is also no consensus as to appropriate timing and dosage.

### Challenging pain scenarios

#### Neuropathic pain

There is increasing evidence that difficult to manage, severe postoperative pain may be acute neuropathic pain (NeP), defined as pain due to damage or disease of the nervous system. Neuropathic pain may be identified using relatively simple questionnaires in the chronic pain setting, but these may not be as reliable in acute NeP. Neuropathic pain is generally poorly responsive to standard analgesics. There are a number of anti-neuropathic medications used in chronic pain states, including anti-depressants, such as amitriptyline, and anti-epileptic drugs including gabapentin, which have been shown to have some efficacy in acute pain.

#### Pain in medical patients

It has become increasingly clear that the prevalence of significant pain in medical inpatients is in the region of 20%, similar to that in patients following surgical procedures. Pain is often poorly assessed and managed in such patients, and this is an area of unmet need in many hospitals. The high prevalence of chronic pain and co-morbidities make effective prescribing for medical patients difficult.

#### Pain in opioid-tolerant patients

Managing acute pain in opioid-tolerant patients is an increasingly common problem. The principles of pain management are unchanged for patients with opioid tolerance, but some key points must be kept in mind. The aim is to prevent withdrawal, deliver adequate analgesia and avoid increases in the background level of opioids at discharge from hospital. This may require close contact with the patient’s GP and careful discharge planning, including appropriate follow-up.

Background slow-release opioids should be continued if possible throughout the inpatient stay. This is particularly important for trans-dermal fentanyl preparations, where significant withdrawal may occur. The partial agonist buprenorphine
may present particular problems when taken in high doses (>10 mg Subutex) for opioid abuse prevention. Other strong opioids are less likely to be effective in this situation and non-opioid analgesics, regional anaesthesia and atypical analgesics may prove helpful. If necessary, Subutex may be ceased in the peri-operative period.

Generally, higher opioid doses than usual will be required to achieve effective analgesia in patients who are already taking opioids. Very high doses of opioids (>200 mg/day morphine oral equivalent) or rapidly increasing doses may result in OIH with worsening pain severity. This may be treated by reducing opioid intake, or by the use of an NMDA-R antagonist such as ketamine. At low doses, ketamine has been shown to reverse both OIH and tolerance in humans and animal models, given subcutaneously or intravenously (0.1–0.2 mg/kg/hour for 24–48 hours). Lower doses are generally well tolerated as psychotomimetic side-effects are directly related to plasma concentration.

**Summary**

Although acute pain following surgery can often be effectively treated following protocols based on a WHO analgesic ladder, there are a significant number of situations where this straightforward approach fails to achieve the desired effect. The WHO ladder was devised to manage cancer pain, which tends to increase with time, whereas post-surgical pain is usually severe initially and gradually resolves — therefore a ‘reversed ladder’ may be a more appropriate concept. Particular care is needed when managing strong opioids perioperatively to avoid exacerbating the problems of opioid misuse and overuse in the community. The remit of inpatient pain management teams now spreads beyond surgery and beyond the inpatient setting, requiring good communication and multidisciplinary working with physicians, primary care teams and chronic pain management colleagues.

**REFERENCES**