

# Multi-Modal Pain Management Strategies in Postsurgical Pain



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## KEY POINTS

- Persistent pain after surgery is relatively common
- Community based opioid use can be associated with poor outcomes
- A Multimodal Approach reduces need for opioids

**P**ain is described by the International Association for the Study of Pain (IASP) as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage”. Although acute pain cannot always be distinguished from chronic pain using time-based definitions, pain is considered chronic if it continues more than 90 days following surgery or injury.

Episodes of acute pain can progress to development of chronic pain in some patients which can seriously impact on a person’s quality of life, wellbeing and livelihood. Therefore, attempts to prevent the development of chronic pain has many benefits, both personal and economic. Chronic postsurgical pain (CPSP) is defined by the International Classification of Diseases 11th Revision (ICD-11) as “pain that develops or increases in intensity after a surgical procedure or a tissue injury and persists beyond the healing process, at least 3 months after the initiating event”. The prevalence of CPSP is high, with up to 23% in a large cohort of pain clinic patients in the UK reported surgery as the inciting event for their pain.<sup>1</sup> There are numerous personal and medical predictive factors for CPSP. However poorly controlled acute postsurgical pain is a consistent risk factor in large scale observational studies.<sup>2</sup>

Given its nature, significant postoperative pain management is primarily

managed in the hospital environment. However, with the advent of ambulatory surgery (hospital stay <24hrs) and enhanced recovery after surgery (ERAS) programmes, patients are discharged to the community increasingly early. They may need ongoing multidisciplinary team input including pharmacists, general practitioners and community nurses to help manage this transition of care. In the USA, earlier discharge from Hospital is associated with more community-based opioid use.

The greater use of opioids in the last two decades with the aim of better pain management in both cancer and non-cancer related pain has led to a dramatic increase in long term opioid use and in unintentional drug induced deaths worldwide. Well recognised adverse events include nausea, vomiting, constipation, pruritis, sedation and opioid induced hyperalgesia. Many patients are started on opioid medications, especially in the postoperative period, with the associated side effects as well as the potential for new persistent use in an opioid naive patient and risk of diversion on discharge from hospital. Hospital stewardship of procedure specific discharge prescribing practice is a key element of controlling community-based opioid use.

Strategies for pain management should ideally be patient centred, harm free and evidence based. We wish to highlight "Acute Pain Management: Scientific Evidence 5th Edition" as an extensive evidence-based resource for acute pain management from the Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine.<sup>3</sup>

The concept of multimodal or balanced analgesia aims to use combinations of analgesics which work via different modes and sites of action to improve patient experience through better pain control and to reduce opioid consumption and the associated adverse effects of opioids in the postoperative period. There is good evidence to support a varied number of nonopioid analgesics, adjuvants and regional anaesthesia techniques as components of multimodal analgesia. It is necessary to balance the expected severity of postoperative pain with the analgesia used and the potential adverse effects. The following is a brief review of some pharmaceutical components of multimodal analgesia and recent evidence around their use. Some agents are only appropriate for Hospital use at this time.

Paracetamol and its intravenous prodrug proparacetamol are effective analgesic and antipyretic agents widely used in the hospital and community settings. Consistent issues identified are non-compliance with safe regular administration within safe doses. As a relatively safe agent, regular use is a bedrock of multimodal regimes. The additional use of paracetamol-opioid combination medications for breakthrough pain should be avoided due to the risk of inadvertent overdose. Evidence has shown that regular paracetamol used as an adjunct to opioids in the postoperative period leads to a reduction in pain scores and opioid consumption, with reduction for up to 3 days found post hip or knee arthroplasty.<sup>4</sup>

The addition of caffeine and or codeine is however useful in the patient transitioning from higher potency opioids.<sup>5</sup>

Non-steroidal anti-inflammatory drugs (NSAIDs), both non selective and COX-2 selective, are used for their analgesic, anti-inflammatory and anti-pyretic effects. Non-selective NSAIDs have good efficacy in the management of acute post-operative pain, acute muscular pain, renal colic, migraine and primary dysmenorrhoea. A Cochrane review found that selective Cox-inhibitors are as effective as non-selective NSAIDs for acute postoperative pain and chronic back pain in particular, with a favourable side effect profile with regards to gastrointestinal bleeding.<sup>6,7</sup> They are relatively contraindicated in those with pre-existing coronary artery disease due to increased risk of cardiac events. Both classes are avoided in patients with acute or chronic renal failure. NSAIDs should be combined with paracetamol for superior analgesia and to reduce opioid consumption.<sup>8</sup> Potential adverse effects, particularly gastric ulceration can be mitigated with co-administration of proton pump inhibitor antacids.

Local and regional anaesthesia techniques form a core part of multimodal analgesia, delivered by both surgeons and anaesthesiologists. Peripheral nerve blocks are frequently used in the perioperative period to reduce medication requirements in the first 24-48hrs, specifically with the use of longer acting local agents such as bupivacaine or ropivacaine. Catheter infusion techniques and the ongoing development of extended release formulations such as liposomal bupivacaine aim to prolong duration of action. An intravenous infusion of lidocaine is another method used, particularly in major surgeries as part of a multimodal approach. Additional benefits mean it is sometimes used in abdominal surgery cases as there is some limited evidence of improved gastrointestinal outcomes such as time to resolution of bowel ileus postoperatively.<sup>9</sup> Despite limited benefits in acute pain management, there evidence that intravenous lidocaine reduces chronic post-surgical pain at 3 months, specifically in breast surgery cases, with research ongoing in this area.<sup>10</sup>

NMDA receptor antagonists such as ketamine target central and peripheral receptor sites and are an important component of multimodal analgesia. At low sub-anaesthetic doses a reduction in postoperative pain and opioid consumption in patients in the first 48hrs can be observed by up to 20%.<sup>11</sup> It is a useful adjunct, often helpful in opioid tolerant patients and is also associated with a reduction in incidence of chronic postsurgical pain.

Dexmedetomidine and Clonidine are alpha adrenoceptor agonists that can bind to presynaptic receptors and inhibit norepinephrine release. They are increasingly used in multimodal analgesia regimes to reduce opioid consumption. Side effects include sedation, drop in blood pressure and evidence for community use is limited.

Magnesium is another intravenous agent which targets NMDA receptors as its primary analgesic mechanism of action, while

potentially having other anti-inflammatory effects via interleukin-6 and tumour necrosis factor modulation. It can be used alone or in conjunction with ketamine for synergistic effects, and has been shown to improve postoperative pain scores up to 24hrs with an opioid sparing effect.<sup>12</sup>

Anticonvulsants can be utilised as perioperative pain medications with Gabapentin and Pregabalin being the most widely used. Gabapentin is often used in combination where persistent postsurgical pain or continued opioid use is observed. They may form part of a hospital discharge prescription regime for short term use with one study looking at the addition of Pregabalin after total hip arthroplasty finding reduced postoperative opioid consumption and for one week after discharge.<sup>13</sup> However, clinicians should consider the increased risk of sedation and dizziness when selecting suitable patients at discharge.

Every patient has a unique subjective experience of pain that needs to be explored and requires patient centred care from the multi-disciplinary team. The medication classes discussed above are some of the numerous options available when deciding on a multimodal analgesia regime, an area with abundant ongoing research looking at both the medication pharmacodynamics and interactions, and their use in relation to specific procedures and patient groups. Each regime should be patient and procedure specific, taking into account factors such as current illness and co-morbidities, procedure location and expected severity of postoperative pain as well as predicted hospital length of stay.

There are still however a small percentage of patients for whom pain is not adequately controlled despite the numerous pain management techniques used. Psychological, social and cultural factors may all be contributing factors and a pain specialist referral is warranted and the need for extended postoperative follow up is an area of interest. Transitional pain services and acute pain clinics are beginning to be employed internationally to support patients with medication tapering after discharge with the aim of reducing persistent opioid use in targeted postoperative patient groups. These services often comprise of a pain medicine specialist, nurse specialist, pharmacist, psychologist and physiotherapist.

With day case surgery and ERAS programmes, patients are often discharged on a combination of analgesics, including a short course of opioids if deemed necessary. This can be a time where patients may be vulnerable to medication errors and side effects due to changes to regular medications and additional new ones. Community pharmacists play an integral role in ensuring the appropriate and safe use of these medications and offer a vital link with other professionals between the inpatient and outpatient settings to help patients optimize their medication regimens and improve their overall health outcomes.

**References available on request**