Acute pain management: scientific evidence, fourth edition, 2015

Summary

- This guideline summary describes the fourth edition of *Acute pain management: scientific evidence*, which was published by the Australian and New Zealand College of Anaesthetists (ANZCA) and its Faculty of Pain Medicine (FPMANZCA) in December 2015.
- The fourth edition summarises the best available evidence on acute pain management, following methods established over the preceding three editions.
- It provides additional information by scoring the quality of and reporting further details on randomised controlled trials and meta-analyses.
- The information is condensed into key messages that provide:
  - concise statements on each topic, showing the highest level of evidence; and
  - clinical practice points based on clinical experience or expert opinion.

In 1999, the first edition of *Acute pain management: scientific evidence* was written by a multidisciplinary committee under the guidance of Michael Cousins and published by the National Health and Medical Research Council (NHMRC).[1] As there has been a substantial increase in the quantity and quality of publications about acute pain management, the Australian and New Zealand College of Anaesthetists (ANZCA) and its Faculty of Pain Medicine (FPMANZCA) have taken responsibility for revising and updating the available evidence every 5 years.[2,3] The fourth edition, which became publicly available in December 2015,[4] will be available in hard-copy soon, but can already be downloaded for free in pdf format from http://www.anzca.edu.au/resources/college-publications.

Development and methods

As with the first three editions, the document aimed to combine a review of the best available evidence on acute pain management with current clinical and expert practice, rather than to formulate specific recommendations for clinical practice. Accordingly, the document summarises the evidence currently available on the management of acute pain from over 8000 references, and presents it in a concise and easily readable form to aid practising clinicians. The document was prepared by following the methods established over the preceding three editions. All evidence is documented according to NHMRC levels of evidence, from Level I (systematic reviews of randomised controlled trials [RCTs]) to Level IV (case series).[5] However, for the first time, this fourth edition scores systematic reviews and RCTs for quality, and reports the numbers of studies included and patients randomised, to allow readers to assess the relevance of the evidence presented. As in previous editions, the document is preceded by a summary list of all key messages (now totalling 669). These key messages provide concise statements on each topic, showing the highest level of evidence, and clinical practice points based on clinical experience or expert opinion. The document also shows the status of each key message in comparison with the previous edition (eg, new, unchanged, strengthened, qualified, or reversed).

The document addresses all aspects of acute pain management. There are sections on:

- the physiology, psychology and the assessment of acute pain;
- analgesic medicines and routes and techniques of their administration (eg, regional techniques, patient-controlled analgesia [PCA]); and
- non-pharmacological techniques (eg, physical therapies, acupuncture and psychological techniques).

Furthermore, specific clinical situations, such as post-operative pain and acute medical and cancer pain, are addressed, as well as acute pain in specific settings (eg, burns units, intensive care units, emergency departments). Pain in children is dealt with for the first time in a detailed section presenting evidence-based management for this complex and challenging group. Other groups covered in detail are pregnant women, older patients, and patients with opioid tolerance or with an addiction. Culturally responsive care for culturally and linguistically diverse patients, with an emphasis on Aboriginal, Torres Strait Islander and Maori peoples, is also addressed.

Post-operative pain management

This brief overview cannot cover all the evidence provided in the document, but focuses on that related to post-operative pain, one of the most common manifestations of acute pain. However, many of the issues related to post-operative pain are translatable to other acute pain scenarios, in particular pain after trauma. Most of the following statements are summaries or direct quotations of the key messages in the fourth edition.[4]

Multimodal analgesia

The overall concept underlying post-operative (and other) acute pain relief is multimodal or "balanced" analgesia, that is, the use of combinations of analgesics or analgesic techniques with different modes or sites of action. Such an approach (eg, combining a non-opioid with an opioid or a regional analgesia technique with a

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doi: 10.5694/mja16.00133

systemic analgesic) improves pain control compared with mainly opioid-based analgesia, and reduces opioid consumption (ie, is "opioid-sparing") and thereby reduces adverse effects.

Opioid-sparing analgesic approaches permit earlier mobilisation and earlier enteral feeding after surgery and so may contribute to early recovery overall. However, providing appropriate analgesia is only one of several elements of "enhanced recovery after surgery (ERAS)" protocols aiming to reduce hospital stays and complication rates. Furthermore, different surgical procedures cause different pain states (eg, musculoskeletal versus visceral) of different severity in different locations.

Procedure-specific post-operative pain management

As the efficacy of analgesics can be different in different surgical settings, pooling of data from various post-operative pain states may ignore the specific effects of a specific analgesic or technique in a specific post-operative setting. Therefore, post-operative pain requires a procedure-specific approach to analgesia. The recognition of this need has led to the development of the Prospect (PROcedure-SPECific post-operative pain managemenT) initiative (http://www.postoppain.org), which provides procedure-specific evidence-based recommendations for the treatment of pain after a wide range of operations.[6,7]

Acute neuropathic pain

In assessing acute pain after surgery and trauma, acute neuropathic pain is often overlooked or its severity underestimated. This has important consequences, as neuropathic pain does not respond to many common analgesics, and requires specific therapeutic approaches. Ketamine, opioids (including tramadol or tapentadol) and $\alpha_2\delta$ ligands (gabapentin or pregabalin) are the preferred systemic treatment options for acute neuropathic pain, as a rapid onset of effect is needed in this setting. Early recognition of neuropathic pain in an acute setting is also relevant, as chronic post-surgical pain and post-traumatic pain often have a neuropathic component. Risk factors that predispose to the development of such pain include the severity of pre-surgical chronic pain and post-surgical acute pain, and intraoperative nerve injury. Chronic pain after surgery and trauma is more common than generally thought, and can lead to significant disability. Diagnosis and subsequent appropriate treatment of acute neuropathic pain might prevent the development of chronic pain.

Preventive analgesia

Some analgesic interventions have an effect on post-operative pain and/or analgesic consumption that exceeds the expected duration of action of the medicine. Such interventions are defined as preventive analgesia. Ketamine and local anaesthetics have such a preventive effect. There are now also data that show that ketamine, certain regional analgesic techniques and possibly calcium channel $\alpha_2\delta$ subunit ligands (gabapentin and pregabalin) prevent the development of chronic post-surgical pain. There are significant associations between psychosocial factors such as anxiety, pain catastrophising, depression, psychological vulnerability and stress and the subsequent development of chronic post-surgical pain.

Regional analgesia and continuous peripheral nerve blocks

There is increasing evidence for the role of regional anaesthesia techniques in providing effective post-operative pain relief. Such techniques are not only preventive as outlined above, but provide overall excellent analgesia with minimal systemic adverse effects and can thereby improve and accelerate recovery. The evidence remains strong for continuous epidural analgesia, in particular after major thoracic and abdominal surgery with improved return of bowel function and overall reduced morbidity and possibly even mortality. However, this technique is underutilised in some parts of the world due to the fear of serious complications, in particular in conjunction with use of anticoagulants, and to the perceived increased workload in managing patients with thoracic epidural analgesia. This has led to increased use of continuous peripheral nerve blocks in the post-operative setting, which, compared with single-injection peripheral nerve blocks, result in improved pain control, decreased need for opioid analgesics, reduced nausea and improved patient satisfaction.

Compared with opioid analgesia, continuous peripheral nerve blocks (regardless of catheter location) provide better post-operative analgesia and reductions in opioid use as well as decreased nausea, vomiting, pruritus and sedation. The use of ultrasound guidance to perform blocks increases block success rates, reduces block performance time and the risk of local anaesthetic toxicity and results in faster onset and longer duration of analgesia compared with localisation using a peripheral nerve stimulator.

Techniques for which there is particularly good evidence include continuous thoracic paravertebral analgesia (for unilateral thoracotomies and after rib fractures) and transversus abdominis plane blocks (after abdominal surgery), as well as a broad range of peripheral nerve blocks of the upper and lower limb (after orthopaedic surgery). After total knee joint replacement, femoral nerve blocks are a proven approach, but there is also increasing evidence to support local infiltration analgesia.

With regard to complications, post-operative neurological dysfunction is often related to patient and surgical factors, and the incidence of neuropathy directly related to regional anaesthesia is rare. Continuous peripheral and regional nerve blocks carry a risk of infection; skin preparation with alcohol-based chlorhexidine and full barrier precautions (including face masks) are recommended for insertion of peri-neural catheters.

Patient-controlled analgesia

Opioids remain an important component of systemic analgesia for the relief of severe pain despite the multiple opioid-sparing approaches. In the early post-operative setting, intravenous opioids delivered via PCA provide better analgesia than conventional parenteral opioid regimens and result in greater patient satisfaction. Adding a background infusion to morphine delivered intravenously via PCA in opioid-naive patients increases the incidence of respiratory depression and does not improve pain relief or sleep, or reduce the number of PCA demands. There is little evidence that any particular opioid delivered via PCA is superior to another in regard to analgesic or adverse effects in general, but individual patients may tolerate one opioid better than another. The safety of PCA use can be significantly improved by hospital-wide safety initiatives ("smart pumps", equipment, guidelines, education, monitoring).

Non-opioid analgesics

There is good evidence to support the use of non-opioid analgesics to complement opioid analgesics for multimodal analgesia; non-steroidal anti-inflammatory drugs (NSAIDs) are superior to paracetamol (and combining both increases efficacy) and COX-2 inhibitors (coxibs) offer safety advantages over non-selective NSAIDs, in particular with regard to platelet dysfunction leading to blood loss. The risk of adverse renal effects of non-selective NSAIDs and coxibs is increased in the presence of factors such as pre-existing renal impairment, hypovolaemia, hypotension and the use of other nephrotoxic agents including angiotensin-converting enzyme inhibitors. Other analgesic options include peri-operative intravenous lignocaine, which has been shown to reduce pain and opioid requirements after abdominal surgery and to decrease nausea, vomiting, duration of ileus and length of hospital stay. Peri-operative intravenous ketamine reduces opioid consumption, time to first analgesic request and post-operative nausea and vomiting compared with placebo. It is particularly helpful in opioid-tolerant patients. Peri-operative administration of $\alpha_2\delta$ ligands reduce post-operative pain and opioid requirements and reduce the incidence of vomiting, pruritus and urinary retention, but increase the risk of sedation. The peri-operative use of systemic α_2-receptor agonists (clonidine and dexmedetomidine) reduces post-operative pain intensity, opioid consumption and nausea without prolonging recovery times, but the frequency and severity of adverse effects (bradycardia and hypotension) sometimes limit their clinical usefulness. Dexamethasone reduces post-operative pain and opioid requirements to a limited extent, but also reduces nausea and vomiting, fatigue, and improves the quality of recovery compared with placebo. Current evidence does not support the use of cannabinoids in acute pain management.

Non-pharmacological strategies

There is some evidence to support non-pharmacological techniques for providing post-operative analgesia. Transcutaneous electrical nerve stimulation (TENS) compared with sham TENS reduces acute pain (procedural and non-procedural), including pain after thoracic surgery. Acupuncture (specifically, auricular acupuncture) reduces post-operative pain and opioid requirements, as well as opioid-related adverse effects compared with a variety of controls. Beneficial effects of acupuncture on post-operative pain have been confirmed in particular after back surgery and ambulatory knee surgery and total knee joint replacement. Psychological (including distraction [music, books, video] and hypnosis), physical (including holding, warming, non-nutritive sucking) and use of sweet solution (sucrose) interventions are particularly beneficial in painful procedures in children and are being used peri-operatively.

Conclusion

The increase in evidence in the area of acute pain management over the past 15 years is impressive. Based on the evidence available, which is summarised in the fourth edition of *Acute pain management: scientific evidence*,[4] physicians can make evidence-based decisions in most acute pain scenarios. Such an approach improves the safety and effectiveness of treatment of patients in acute pain, thereby reducing pain and suffering. These guidelines are even relevant to primary care physicians, who may influence outcomes in these patient populations.

However, a significant gap remains between evidence and practice in the area of acute pain management. It is the challenge for all health care professionals to reduce this gap to benefit our patients.

Competing interests: The Anaesthesiology Unit of the University of Western Australia, chaired by Stephan Schug, but not he privately, has received research and travel funding and speaking and consulting honoraria from bioCSL, Bionomics, Eli Lilly, Gruenenthal, Janssen Pharmaceuticals, Mundipharma, Pfizer, Phosphagenics and iX Biopharma within the past 5 years.

Provenance: Commissioned; externally peer reviewed. ■

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