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REVIEW

The transition of acute postoperative pain to chronic pain: Part 2 – Limiting the transition

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SUMMARY

The transition of acute perioperative pain to pathological chronic post-surgical pain (CPSP) is a complex and poorly understood process. The Anaesthetist plays a pivotal role in the early recognition of patients with chronic pain and in the identification of factors that may lead to suboptimal pain control in the perioperative period. Multimodal pharmacological strategies, psychological strategies, modified surgical techniques, procedure-specific postoperative pain management, and enhanced postoperative recovery programmes are all used to prevent persistent acute postoperative pain. These are discussed. The establishment of a core minimum dataset for future epidemiologic studies is emphasised.

1. Introduction

Mounting evidence that tissue injury often results in changes to the nervous system function has provided a new understanding of mechanisms that explain how surgery can often lead to chronic pain.[1] On average, one in five patients undergoing surgery will develop chronic post-surgical pain.[1] Interactions between the nervous and immune systems are complex. These result in peripheral and central sensitization that is crucial to the development of chronic pain. The Anaesthetist plays a pivotal role in the early recognition of patients with chronic pain and in identification of factors that may lead to suboptimal pain control in the perioperative period.[2] Careful planning of the patient's care throughout this period can mitigate these factors. Multimodal strategies have been adopted to manage preoperative, intraoperative, and postoperative pain.[3] These are discussed. This review is based on an extensive search of the literature in relation to the topics covered without strict inclusion or exclusion criteria in the search strategy.

2. Prevention or limitation strategies

Pre-emptive analgesia whereby preoperative anti-nociceptive treatment prevents surgery-induced central sensitization and increased postoperative pain intensity has not proven clinically effective.[3] The extent to which perioperative peripheral nociceptive inputs contribute to central sensitization and postoperative pain remains unknown.[3] Central sensitization can be induced by factors other than the peripheral nociceptive barrage associated with incision, and by other noxious intraoperative events.

Preventive analgesia focuses on attenuating the impact of the peripheral nociceptive barrage associated with noxious perioperative stimuli, in order to reduce pain and analgesic requirements well beyond the surgical period.[3] To avoid 'pain chronification' adequate therapy of the pre-existing pain should be carried out.[4] For example, recent preliminary results show that after limb amputation, prolonged and individualized (from 4 to 83 days) perineural infusion of local anaesthetic significantly reduces the incidence of phantom pain (16% instead of the 67% usually reported with shorter lasting therapeutic interventions).[5]

There is an increased postoperative morbidity associated with opioid-only strategies (such as nausea, vomiting, sedation, pruritus, constipation, urinary retention, and respiratory depression).[3] Long-term consequences of perioperative opioids (development of chronic postsurgical pain syndromes, hyperalgesia, and immunomodulation) are increasingly being recognized.[6] Opioid medications tend not to be effective in relieving movement-evoked pain. Combining them with non-opioid analgesics or limiting their use enhances recovery.[7] Patient-controlled analgesia (PCA)-intravenous, PCA-oral, patient-controlled regional anaesthesia, or patient-controlled epidural analgesia is used to empower patients to play a role in their postoperative pain management. Empirical evidence derived from clinical trials shows that the use of multi-modal analgesic therapy using a combination of analgesic agents, each

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with a different mechanism of action, is effective in blocking the various inputs/receptors related to neural and inflammatory processes.[3]

Several studies using quantitative sensory testing and specific questionnaires have reported a major neuropathic component in CPSP.[5] With surgical repair after nerve damage, cofactors like poor capacity of nerve regeneration (from suspected genetic origin), decreased pain tolerance (from altered endogenous pain processing) and a particular psychological profile played a major role as shown in the 33% of patients who developed CPSP.[5] More intraoperative data on handling of tissue and nerves needs to be collected.

2.1. Psychological strategies

Cognitive-behavioural therapy, acceptance commitment therapy, electromyographic biofeedback, hypnosis, and coping strategies are some of the psychological strategies used (Table 1). New treatment approaches focus on the extinction of aversive memories, and the restoration of the body image and normal brain function. These approaches include brain stimulation, mirror training, virtual reality applications, or behavioural extinction training.[8]

2.2. Multimodal pharmacological strategies

Multimodal (or "balanced") analgesia therefore represents an approach to preventing postoperative pain where the patient is administered a combination of opioid and non-opioid analgesic drugs that act at different sites within the central and peripheral nervous systems in an effort to minimize opioid use and decrease opioid-related side effects (Table 1).[6] Multimodal analgesia uses a combination of delivery routes (i.e. enteral, parenteral, epidural, intrathecal). These are administered at variable time points (i.e. preoperative, intraoperative, and postoperative) to optimize outcomes in the treatment of acute pain and in the prevention of chronic pain.[9] Many clinical studies have reported an opioid-sparing effect using a wide variety of non-opioid adjuvants (i.e. local anaesthetics, non-steroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase-2 inhibitors, paracetamol, ketamine, clonidine, dexmedetomidine, adenosine, gabapentin, pregabalin, glucocorticoids, esmolol, neostigmine, and magnesium).[6,10] Implementing a multi-modal regimen at the outset can diminish the unwanted adverse effects of opioid analgesics and reduce intraoperative and long-term tolerance.[3]

Paracetamol (acetaminophen) modestly inhibits peripheral prostaglandin synthesis; it centrally blocks the formation and release of prostaglandins inhibiting action of endogenous pyrogens on the heat-regulating centres in the brain.[3] Recent research suggests that a COX-3 pathway inhibits a central prostaglandin synthesis in the hypothalamus and decreases prostaglandin E in cerebrospinal fluid, to produce analgesic and antipyretic effects.[3] The optimal use of paracetamol (acetaminophen) by mouth, rectally, or intravenously (as the prodrug proparacetamol) can improve pain control.[6]

Adverse effects of NSAIDs include gastric ulceration, haemorrhage, renal dysfunction, and platelet inhibition[3]; NSAIDs should be used cautiously in patients with renal dysfunction, sepsis, end-stage liver disease, or cardiac disease.[3] 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 (no platelet inhibition), and are presumed to have less gastrointestinal toxicity (gastropathy is approximately half of the NSAIDS).[6] Of note is that the COX-2 selective inhibitors (celecoxib, etoricoxib) do not inhibit bone healing.[3] Currently celecoxib, etoricoxib, and lumiracoxib (in low doses) are used. Parecoxib is the only parenterally administered coxib available to date.[6]

Table 1
Prevention and management of risk factors in acute perioperative pain for developing chronic pain.

Preoperative prevention and management	Individualised education of patient and clinical staff (about procedure and intended pain management) Supply relevant patient information Address patient attitudes and concerns Identify operative procedures that cause severe pain Aggressively optimise analgesia in acute injury and pre-operative phase and extend into postoperative period Use standardized pain evaluation and treatment protocols Identify patients with modifiable risk factors for development of acute persistent and ultimately chronic pain, follow up and manage after discharge Screen and provide perioperative psychological pain-management interventions where relevant
Intraoperative prevention and management	Modify known surgical risk factors Use least painful surgical approach with acceptable exposure Prevent nerve and tissue damage Provide protective multimodal opioid-sparing analgesic pharmacotherapy Add afferent neural blockade where appropriate (e.g. epidural analgesia for thoracotomy and major laparotomy and paravertebral blockade for breast surgery) Use local anaesthesia at incision sites Use a procedure-specific analgesic regimen (from the PROSPECT group wherever possible)
Postoperative prevention and management	Measure pain levels at rest and with movement Aggressively optimise analgesia with protective multimodal opioid-sparing analgesic pharmacotherapy (consider use of gabapentin) (keep pain levels <5/10 on days 1–5 postoperatively) Use a multidisciplinary enhanced postoperative recovery programme Use evidence-based adjustments to the use of nasogastric tubes, drains, and urinary catheters, preoperative bowel preparation, and early initiation of oral feeding and mobilization Perform a bedside neurological examination if neuropathic pain is suspected Continue analgesia well into postoperative period
Discharge plan	Individualise discharge analgesic packages and home follow-up

Inflammatory responses contribute to pain, fatigue and organ dysfunction. They can be modified pharmacologically by preoperative glucocorticoids.[7] Whilst multiple studies investigating the role of NSAIDs and steroids for acute postoperative pain have consistently shown benefit, many of these studies have not specifically investigated their longer term effects on the development of chronic pain.[9]

Low-dose ketamine (N-Methyl-D-aspartate antagonist) in the range of 0.25–0.5 mg/kg as an initial bolus followed by 50–500 μg/kg/h is used as an adjuvant for postoperative analgesia and for the reduction of exogenous opioid-induced hyperalgesia.[3] Ketamine in sub-anaesthetic doses is effective in reducing morphine requirements in the first 24 h after surgery.[6] More research into the effectiveness of dextromethorphan, another N-Methyl-D-aspartate antagonist is needed. Ketamine may attenuate tolerance to opioids.