Management of Perioperative Pain

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October 27, 2017

Nothing to disclose
Learning Objectives

• Discuss the multidisciplinary approach of Enhanced Recovery after Surgery (ERAS) to improve clinical outcomes and reduce costs
• Distinguish three ERAS elements where pharmacy can have an impact to improve patient postoperative care
• Identify three pre-existing conditions / characteristics or pre-existing therapies, which can result in poor postoperative pain control and potentially lead to chronic pain
  – Assess why and how to prevent or minimize the impact on postoperative pain management

Learning Objectives

• Distinguish between the three parenteral NSAIDs
• Identify which are administered IV push versus which are administered by IVPB or intermittent infusion
Guidelines on the Management of Postoperative Pain

Management of Postoperative Pain: A Clinical Practice Guideline
From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists’ Committee on Regional Anesthesia, Executive Committee, and Administrative Council

• 80% patients who undergo surgical procedures experience acute postoperative pain
• 75% with postoperative pain report the intensity as moderate, severe, or extreme
• Less than half report adequate postoperative pain relief

Recommendations

• Preoperative Education and Perioperative Pain Management Planning
  – “The panel recommends that clinicians provide patient and family-centered, individually tailored education to the patient (and/or responsible caregiver), including information on treatment options for management of postoperative pain, and document the plan and goals for postoperative pain management.”
  – “The panel recommends that the parents (or other adult caregivers) of children who undergo surgery receive instruction in developmentally-appropriate methods for assessing pain as well as counseling on appropriate administration of analgesics and modalities.”
  – “The panel recommends that clinicians conduct a preoperative evaluation including assessment of medical and psychiatric comorbidities, concomitant medications, history of chronic pain, substance abuse, and previous postoperative treatment regimens and responses, to guide the perioperative pain management plan.”
Preoperative Education and Perioperative Pain Management Planning

- “The panel recommends that clinicians adjust the pain management plan on the basis of adequacy of pain relief and presence of adverse events”

Methods of Assessment

- “The panel recommends that clinicians use a validated pain assessment tool to track responses to postoperative pain treatments and adjust treatment plans accordingly.”

General Principles Regarding the Use of Multimodal Therapies

- “The panel recommends that clinicians offer multimodal analgesia, or the use of a variety of analgesic medications and techniques combined with **non-pharmacological interventions**, for the treatment of postoperative pain in children and adults.”

Use of Systemic Pharmacological Therapies

- “The panel recommends oral over intravenous (i.v.) administration of opioids for postoperative analgesia in patients who can use the oral route.”
- “The panel recommends that clinicians avoid using the intramuscular route for the administration of analgesics for management of postoperative pain.”
- “The panel recommends that i.v. patient-controlled analgesia (PCA) be used for postoperative systemic analgesia when the parenteral route is needed.”
- “The panel recommends against routine basal infusion of opioids with i.v. PCA in opioid-naive adults.”
• Use of Systemic Pharmacological Therapies
  – “The panel recommends that clinicians provide appropriate monitoring of sedation, respiratory status, and other adverse events in patients who receive systemic opioids for postoperative analgesia.”
  – “The panel recommends that clinicians provide adults and children with acetaminophen and/or nonsteroidal anti-inflammatory drugs (NSAIDs) as part of multimodal analgesia for management of postoperative pain in patients without contraindications.”
  – “The panel recommends that clinicians consider giving a preoperative dose of oral Celecoxib in adult patients without contraindications.”
  – “The panel recommends that clinicians consider use of Gabapentin or Pregabalin as a component of multimodal analgesia.”
  – “The panel recommends that clinicians consider i.v. Ketamine as a component of multimodal analgesia in adults.”
  – “The panel recommends that clinicians consider IV Lidocaine infusions in adults who undergo open and laparoscopic abdominal surgery who do not have contraindications.”

Inadequately Managed Postoperative Pain

• Negatively affects quality of life
• Negatively affects function and functional recovery
• Increases risk of post-surgical complications
• Risk of persistent post-surgical pain

Inadequately Managed Postoperative Pain

- Increased resource utilization
- Increased healthcare costs related to longer hospital days
- Higher rates of readmission

Anesthesiology. 2004;100: 1573-1581.
Anesthesiology. 2000; 93:1123-1133.

Persistent postsurgical pain: risk factors and prevention
Henrik Kehlet, Troels S Jensen, Clifford J Woolf
Lancet 2006; 367: 1618–25

Acute postoperative pain is followed by persistent pain in 10–50% of individuals after common operations, such as groin hernia repair, breast and thoracic surgery, leg amputation, and coronary artery bypass surgery. Since chronic pain can be severe in about 2–10% of these patients, persistent postsurgical pain represents a major, largely unrecognized clinical problem. Iatrogenic neuropathic pain is probably the most important cause of long-term postsurgical pain. Consequently, surgical techniques that avoid nerve damage should be applied whenever possible. Also, the effect of aggressive, early therapy for postoperative pain should be investigated, since the intensity of acute postoperative pain correlates with the risk of developing a persistent pain state. Finally, the role of genetic factors should be studied, since only a proportion of patients with intraoperative nerve damage develop chronic pain. Based on information about the molecular mechanisms that affect changes to the peripheral and central nervous system in neuropathic pain, several opportunities exist for multimodal pharmacological intervention. Here, we outline strategies for identification of patients at risk and for prevention and possible treatment of this important entity of chronic pain.

- Postsurgical chronic pain is the consequence either of ongoing inflammation or more commonly, a manifestation of neuropathic pain."
  - Peripheral and central neuroplastic changes that appear as a result of tissue and nerve injury.
- Immediate postoperative period
  - Direct activation of nociceptors (scalpel blade cutting through skin)
  - Inflammatory pain (heightened pain response to tissue injury and inflammation)
  - Injury to nerves (Major nerves trespass the surgical field of most surgical procedures associated with chronic pain)
Persistent postsurgical pain: risk factors and prevention

Henrik Kehlet, Troels S Jensen, Clifford J Woolf

Lancet 2006; 367: 1618–25

- **Inflammatory Pain**
  
  - “The clinical picture is dominated by spontaneous resting and breakthrough pain referred to the site of surgery and the surrounding tissues.”
  
  - “Movement or touching of the wound site, breathing, coughing, and gastrointestinal motility can all evoke flares of pain. Stimulus-evoked hypersensitivity is present both in the injured area and the surrounding non-injured tissue.”
  
  - “Most patients respond well to opiates and COX inhibitors.”
    
    - “In a subset of patients, a continuous inflammatory response, such as after inguinal mesh hernia repair, can contribute to a maintained inflammatory pain.”

- **Surgical Nerve Injury**
  
  - “If nerves are injured during surgery, a neuropathic component of the pain might develop immediately and then persist in the absence of any peripheral noxious stimulus or ongoing peripheral inflammation.”
  
  - “This pain, once established, is likely to be resistant to COX inhibitors.”
    
    - “Signs of neurological damage, in the form of hypoaesthesia, have been reported after mastectomy, hernia repair, and mandibular osteotomy. Extensive nerve damage is frequent in thoracotomy, since use of a rib retractor blocks intercostal nerve conduction by 50–100% in segments close to the incision, according to the findings of late intraoperative electromyography.”

- **Factors that might predispose a surgical patient to develop chronic pain**
  
  - Preceding pain
    
    - Preamputation pain
    
    - Postherpetic neuralgia often preceded by severe zoster pain
  
  - Psychosocial factors
    
    - Expectation of pain, fear, past memories
    
    - Catastrophising – tendency to exaggerated pessimism about outcome
      
      - Correlated with the intensity of acute, but not of chronic postoperative pain
    
    - Preoperative anxiety correlates with postoperative pain experience
  
  - Genetic susceptibility
    
    - Sensitivity to physiological nociceptive and clinical pain differs considerably between surgical patients
    
    - Genetic difference to the analgesics
    
    - High Catecholamine-O-MethylTransferase (COMT) activity correlates with a risk of developing chronic temporomandibular joint pain
  
  - Age
    
    - Post-herniorrhaphy pain, older patients have reduced risk of developing chronic pain

- **The intensity of acute postoperative pain correlates with the risk of chronic postsurgical pain**
Persistent postsurgical pain: risk factors and prevention
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Surgical Technique
– Groin Hernia Repair
  • Laparoscopic herniorrhaphy – Decrease the nerve damage and pain compared to open surgery
  • Use of a light-weight mesh for inguinal hernia repair to reduce inflammatory response
– Mastectomy
  • Preservation of the intercostal brachial nerve (sentinel lymph node biopsy)
– Thoracotomy
  • Muscle sparing technique results in less nerve damage and chronic pain than a posterolateral approach
• Pre-emptive and aggressive multimodal analgesia

Catastrophizing: a predictive factor for postoperative pain

Keywords: Pain; Surgery; Analgesia; Catastrophizing; Anxiety

Abstract
BACKGROUND: Postsurgical pain is a major cause of delayed recovery and discharge after surgery. A significant proportion of patients develop chronic postsurgical pain, which affects their quality of life. Cognitive and psychological factors are reported to play a significant role in the severity of reported postsurgical pain. High levels of catastrophizing are associated with a heightened pain experience and appear to contribute to the development of chronic pain. This article describes the concept of pain catastrophizing, its association with postsurgical pain, and its potential role in the management of postsurgical pain and postsurgical quality of life.

METHODS: Data for this review were identified from MEDLINE, EMBASE, and PsycINFO. Reference lists of selected articles were cross-searched for additional literature.

RESULTS: High catastrophizing levels were found to be associated with increased pain severity, increased incidence of development of chronic pain, and poorer quality of life after surgery. There was no consensus on the relation between catastrophizing and analgesia consumption.

CONCLUSIONS: Identifying and reducing catastrophizing levels can help to optimize pain management in surgical patients.

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Preoperative Anxiety and Catastrophizing
A Systematic Review and Meta-analysis of the Association With Chronic Posturgical Pain

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Clin J Pain • Volume 28, Number 9, November/December 2012

Objectives: Anxiety and pain catastrophizing predict acute postoperative pain. However, it is not well established whether they also predict chronic posturgical pain (CPSM). The aim of this systematic review and meta-analysis was to investigate whether high levels of preoperative anxiety or pain catastrophizing are associated with an increased risk of CPSM.

Methods: Electronic search databases included PubMed and PsychINFO. Additional literature was obtained by reference tracking and expert consultation. Studies from 1938 until October 2010, investigating the association between preoperative anxiety or pain catastrophizing and CPSM in adult surgery patients, were assessed. The primary outcome was the presence of pain at least 3 months postoperatively.

Results: Twenty-nine studies were included; 14 instruments were used to assess anxiety or pain catastrophizing. Sixteen studies (55%) reported a statistically significant association between anxiety or pain catastrophizing and CPSM. The proportion of studies reporting a statistically significant association was 67% for studies of musculoskeletal surgery and 36% for other types of surgery. There was no association with study quality, but larger studies were more likely to report a statistically significant relationship. The overall pooled odds ratio, on the basis of 15 studies, ranged from 1.05 (95% confidence interval, 0.70-1.29) to 2.00 (95% confidence interval, 1.49-2.85). Pain catastrophizing might be of higher predictive utility compared with general anxiety or more specific pain-related anxiety.

Discussion: There is evidence that anxiety and catastrophizing play a role in the development of CPSM. We recommend that anxiety measures should be incorporated in future studies investigating the prediction and transition from acute to chronic posturgical pain.

Key Words: anxiety, catastrophizing, risk factor, postsurgical, chronic pain

Rates and risk factors for prolonged opioid use after major surgery: population based cohort study

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BMJ 2014;348:g1251 doi: 10.1136/bmj.g1251 (Published 11 February 2014)

Abstract
Objective To describe rates and risk factors for prolonged postoperative use of opioids in patients who had not previously used opioids and undergoing major elective surgery.

Design Population based retrospective cohort study.

Setting Acute care hospitals in Ontario, Canada, between 1 April 2003 and 31 March 2010.

Participants 39,140 patients aged 65 years or older who had major elective surgery, including cardiac, intra-abdominal, and pelvic procedures.

Main outcome measure Prolonged opioid use after discharge, as defined by ongoing patient prescriptions for opioids for more than 90 days after surgery.

Results Of the 39,140 patients in the entire cohort, 49.2% (n=19,296) were discharged from hospital with an opioid prescription, and 3.1% (n=1,258) continued to receive opioids for more than 90 days after surgery. Following risk adjustment with multivariable logistic regression modeling, patient related factors associated with significantly higher risks of prolonged opioid use included younger age, lower household income, specific comorbidities (diabetes, heart failure, pulmonary diseases), and use of specific drugs preoperatively (benzodiazepines, selective serotonin reuptake inhibitors, angiotensin converting enzyme inhibitors). The type of surgical procedure was also highly associated with prolonged opioid use. Compared with open radical prostatectomies, both open and minimally invasive thoracic procedures were associated with significantly higher risks (odds ratio 2.61, 95% confidence interval 2.03 to 3.31 and 1.95 1.36 to 2.78, respectively). Conversely, open and minimally invasive major gynecological procedures were associated with significantly lower risks (0.73, 0.55 to 0.98 and 0.45, 0.33 to 0.62, respectively).

Conclusions Approximately 9% of previously opioid naïve patients continued to use opioids for more than 90 days after major elective surgery. Specific patient and surgical characteristics were associated with the development of prolonged postoperative use of opioids. Our findings can help better inform understanding about the long term risks of opioid treatment for acute postoperative pain and define patient subgroups that warrant interventions to prevent progression to prolonged postoperative opioid use.

- Population based retrospective cohort study
- Opioid Naïve patients
- 39,140 Patients
- 66 years and older
- Outcome measure – prolonged opioid use after discharge
- Discharged with opioids – 49.2%
- Opioids continues greater than 90 days – 3.1%
- Adjusted risk factors
  - Younger age
  - Lower household income
  - Comorbidities (DM, CHF, Pulmonary Disease)
  - Preoperative medications (benzodiazepines, SSRIs, ACEI)
  - Both open and minimally invasive thoracic procedures
Buprenorphine

• Indications
  – Opioid abuse disorder (SL and Implant)
  – Acute pain (Injectable)
  – Chronic pain (Transdermal and Buccal film)
Opioid Abuse Disorder Formulations

Table 1: Available Dosages of Buprenorphine/Naloxone Combination Products

<table>
<thead>
<tr>
<th>Suboxone SL Tablet</th>
<th>Suboxone SL Film</th>
<th>Zubzolv SL Tablet</th>
<th>Bunavail Buccal Film</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 mg/0.5 mg</td>
<td>2 mg/0.5 mg</td>
<td>1.4 mg/0.36 mg</td>
<td>N/A</td>
</tr>
<tr>
<td>4 mg/1 mg</td>
<td>4 mg/1 mg</td>
<td>N/A</td>
<td>2.1 mg/0.3 mg</td>
</tr>
<tr>
<td>8 mg/2 mg</td>
<td>8 mg/2 mg</td>
<td>5.7 mg/1.4 mg</td>
<td>4.2 mg/0.7 mg</td>
</tr>
<tr>
<td>12 mg/3 mg</td>
<td>8 mg/2 mg + 2 mg/0.5 mg films</td>
<td>N/A</td>
<td>6.3 mg/1 mg</td>
</tr>
</tbody>
</table>

*a buprenorphine dose/naloxone dose

Pharmacological and Pharmacokinetic Characteristics of Buprenorphine

• Dehydroxylated phenanthrene
  – Chemically similar to hydrocodone, oxycodone, hydromorphone
  – Partial agonist at the μ–opioid receptor (MOR)
    • Activate MOR at low to moderate doses
      – Comparable analgesia to full μ agonist
    • Ceiling dose – will not yield increase analgesia or euphoria (ceiling on retention of carbon dioxide theoretically lowering overdose risk)
  – Antagonist at κ receptors
Pharmacological and Pharmacokinetic Characteristics of Buprenorphine

- Highest affinity of any opioid on the MOR
- Buprenorphine can displace full opioid agonists
- Resistant to displacement by full opioid agonists
- Slow dissociation rate (166 minutes)
- Half-life of 25-45 hours
- High lipophilicity
- Resulting in very slow elimination over a 2-3 day period

Trauma or Surgical Patient

- Managing pain in the patient who is chronically using Buprenorphine
  - Full opioid agonist administered to control acute pain will not remove or replace Buprenorphine from the receptor
  - If Buprenorphine is stopped and elimination is complete (after 2-3 days) then the new full μ agonist opioid will occupy all available MORs.
    - This sudden transition could increase side effects and could result in opioid-induced respiratory depression
Elective Surgery

- Time to taper a patient off of Buprenorphine
  - Substance Abuse and Mental Health Services Administration (SAMHSA) recommends gradually over 2-4 weeks prior to surgery
  - Hospital can then utilize its perioperative pain management plan according to their care paths or orders
  - When full μ agonists are no longer required for post surgical pain then Buprenorphine reintroduced by the patient’s treatment physician. (begin communication with treatment physician as early as possible)
  - Aware the patient may require higher than usual μ agonist doses due to tolerance history

Same Day Surgery

- Unable to taper
- Requires 2-3 days to clear the Buprenorphine
- Three options depending on anticipated level of pain
  - **Mild to moderate** acute pain anticipated – Continue Buprenorphine and add non-opioid analgesics
  - **Moderate** acute pain anticipated – Administer intravenous Buprenorphine
  - Anticipate **severe** acute pain – stop Buprenorphine and administer full μ agonist short acting opioids (**Fentanyl** or **Hydromorphone**) and carefully titrate until the Buprenorphine is cleared (Once cleared may have to begin tapering)
    - Maximize nonopioid adjuvant analgesics and/or nerve blocks
  - Patient should remain hospitalized at least for 3 days after stopping the Buprenorphine
  - **Sending home the patient on large doses of full agonists while the MOR is blocked by the Buprenorphine is very dangerous**
  - Refer to the patient’s treatment physician for conversion back to Buprenorphine therapy. Start communication prior to surgery if possible.
Buprenorphine from Non-medical Sources

• If patient does not disclose then would require very large doses of full agonist opioids during and after surgery
  – “Overcome low intrinsic activity and high binding affinity”
  – After the Buprenorphine is cleared then patient would be at risk for respiratory depression
  – Screen for Buprenorphine use prior to surgery?


To Stop or Not, That Is the Question

Acute Pain Management for the Patient on Chronic Buprenorphine

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• “The management of acute perioperative pain in patients on chronic Buprenorphine as opioid maintenance therapy is a complex process.”
Naltrexone

• Pure opioid antagonist that competes and displaces opioids at opioid receptor sites.
• Dosage forms
  – Naltrexone XR - IM 380 mg monthly injection
  – Naltrexone - Oral 50mg tablets
• Uses
  – Alcohol dependence
  – Rapid Opioid Detoxification
  – Opioid dependence

Challenges in the Perioperative Management of the Patient Receiving Extended-Release Naltrexone

Christopher Curatolo, MD, MEM, and Muoi Trinh, MD, MPH

Patients receiving extended-release (XR) naltrexone who are having surgery present unique challenges to anesthesia providers, the most obvious of which is an altered response to the effects of opioid agonists. Based on the timing of the last XR naltrexone dose, patients may be refractory to the effects of opioid agonists or potentially more sensitive to dangerous side effects due to receptor upregulation and hypersensitivity. Complicating matters, redosing XR naltrexone soon after opioid use may precipitate opioid withdrawal. We present a case of a 22-year-old woman receiving XR naltrexone for a history of heroin abuse undergoing a thyroidectomy and neck dissection. We discuss the intraoperative and postoperative anesthetic and analgesic planning, as well as solutions to some of the challenges these patients pose. (A&A Case Reports. 2014;3:142–4.)

• Last received XR Naltrexone approximately 3.5 weeks prior to scheduled procedure
• Dexamethasone IV 8mg prior to surgical incision
• General anesthesia – Succinylcholine 100mg, propofol 150mg and Remifentanil 150mg
• Anesthesia was maintained with 60% nitrous oxide along with Ketamine 2mg/kg/hr along with propofol 30-40mcg/kg/min and Remifentanil 0.2-0.25mcg/kg/min for duration of the surgery (4 hours)
• Prior to emergence from anesthesia an ultrasound-guided unilateral superficial cervical plexus block with Bupivacaine 0.25% 15ml.
• Acetaminophen 1gm IV
Naltrexone/Bupropion

• Naltrexone (opioid antagonists) and Bupropion (antidepressant dopamine/norepinephrine reuptake inhibitor)

• Indication: Obesity, or overweight in the presence of at least one weight-related comorbidity

• Mechanism of Action: Act to regulate food intake by increasing the firing rate of the hypothalamic Pro-opiomelanocortin neurons (appetite regulatory center) and the mesolimbic circuit (rewards system)

Micromedex 2017

Perioperative Pain Management of a Patient Taking Naltrexone HCl/Bupropion HCl (Contrave): A Case Report

Allen Ninh, BS, Sang Kim, MD, and Andrew Goldberg, MD

A 42-year-old obese woman (body mass index = 30.2 kg/m²) presented for urgent anterior cervical disectomy and fusion. She had been taking oral naltrexone-bupropion extended-release (Contrave, Orexigen Therapeutics Inc, La Jolla, CA) for the past 6 months and continued using it until 12 hours preoperatively. Despite discontinuation of this medication, and employing an intraoperative and postoperative multimodal analgesia strategy, immediate pain control was inadequately achieved. Patients taking opioid antagonists who present for surgery pose unique challenges to the anesthesiologist and require extensive preoperative interdisciplinary discussions and planning for pain control throughout the perioperative period. (A&A Case Reports. 2017:XX:00-00.)

• Naltrexone complicates perioperative pain management of obese patients undergoing bariatric or orthopedic surgeries.
• Postoperative pain management: Hydromorphone PCA patient bolus 0.3mg with lockout of 8 minutes. Acetaminophen IV 1000mg every 6 hrs and Diazepam 5mg PO as needed because of the history of anxiety.
• Pt experienced a single episode of over sedation and O2 desaturation to 83% using the PCA to reduce her 8/10 severe pain. (Step-Down Unit)
• Desaturation was suspected to be cause by undiagnosed OSA
• Pain management team was hesitant to increase the PCA dose due to the episode of desaturation.
• Currently, there are no specific recommendations for the perioperative management of patients taking Naltrexone / Bupropion
Addiction
(Substance Use Disorder)

• Characterized by the four C’s
  – **Craving** for the substance
  – **Compulsive** use
  – **Control** or the lack of control over substance use
  – **Continued** use despite harm

Dependence

• Psychological Dependence
  – Habituation or a continued desire for the drug even after physical dependence is gone

• Physical Dependence (ie. Opioid)
  – Rapid dose reduction in opioid will cause withdrawal symptoms
    • Hypertension, tachycardia, diaphoresis, and abdominal cramping

• These patients should not be labeled as drug seeking or addicts
Tolerance

• Intrinsic Tolerance
  – Pre-existing insensitivity, genetically determined, prior to drug exposure
  – Insensitivity due to pharmacogenetic makeup
  – Genetic Variability in density of opioid receptors, and receptor affinity

• True Tolerance
  – Acquired after multiple opioid exposures
  – Pharmacokinetic, pharmacodynamic and long term

Opioid Tolerance Development: A Pharmacokinetic/Pharmacodynamic Perspective

Emily O. Dumas1,2 and Gary M. Pollack1

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Abstract. The opioids are commonly used to treat acute and severe pain. Long-term opioid administration eventually reaches a dose ceiling that is attributable to the rapid onset of analgesic tolerance coupled with the slow development of tolerance to the untoward side effects of respiratory depression, nausea and decreased gastrointestinal motility. The need for effective-long term analgesia remains. In order to develop new therapeutic and novel strategies for use of current analgesics, the processes that mediate tolerance must be understood. This review highlights potential pharmacokinetic (changes in metabolite production, metabolizing enzyme expression, and transporter function) and pharmacodynamic (receptor type, location and functionality; alterations in signaling pathways and cross-tolerance) aspects of opioid tolerance development, and presents several pharmacodynamic modeling strategies that have been used to characterize time-dependent attenuation of opioid analgesia.

KEY WORDS: opioid; pharmacodynamics; pharmacokinetics; tolerance.

DOI: 10.1208/s12248-008-9056-1
Perioperative Pain Management in the Opioid-Tolerant Patient With Chronic Pain: An Evidence-Based Practice Project
Karen M. Dykstra, BSN, RN, CPAN

According to the Institute of Medicine (IOM) report on pain, chronic pain affects an estimated 116 million American adults and costs the nation more than $600 billion each year in medical treatment and lost worker productivity. Many individuals with chronic pain undergo surgical procedures. Safe and effective treatment of their postoperative pain can present a significant challenge to the health care team but is essential to their optimal recovery. Administration in a community hospital in central Pennsylvania identified a need to improve the care of their patients with chronic pain and supported a hospital-wide initiative to address various aspects of this population's hospital experience. This article presents the first phase of an evidence-based practice project that focused on improving the perioperative pain management in patients with chronic pain who receive long-acting opioids for the treatment of chronic pain before admission for surgery.

Table 2. Evidence-Based Practice Recommendations for Perioperative Pain Management in Patients Who Receive Long Term Opioid Therapy for Chronic Pain

- Ensure that patient takes his/her maintenance opioid dose(s) before surgery.
- Consider the patient's preoperative baseline opioid requirements when prescribing postoperative opioid analgesia. Expect a higher opioid requirement.
- Consider using a basal rate with PCA orders if not reordering the modified-release or long-acting opioid that the patient took preoperatively.
- Use the opioid conversion chart to assist with prescribing an appropriate basal rate (Table 3).
- Consider using a multimodal analgesia approach.
- Prescribe pre- and postoperative use of scheduled nonopioid analgesics.
- A pain service consultation is highly recommended to assist with the development of a pain management plan and discharge recommendations.
- Write the order for the consultation when the patient arrives in Short Stay Unit.

PCA, patient-controlled analgesia.

Intraoperative Ketamine Reduces Perioperative Opiate Consumption in Opiate-dependent Patients with Chronic Back Pain Undergoing Back Surgery
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Anesthesiology 2010; 113:639 - 46

- Results: “Total morphine consumption (morphine equivalents) was significantly reduced in the treatment group 48 h after the procedure. It was also reduced at 24 h and at 6 weeks. The average reported pain intensity was significantly reduced in the post anesthesia care unit and at 6 weeks. The groups had no differences in known Ketamine or opiate related side effects.”

- Conclusions: Intraoperative Ketamine reduces opiate consumption in the 48-h postoperative period in opiate-dependent patients with chronic pain. Ketamine may also reduce opioid consumption and pain intensity throughout the postoperative period in this patient population. This benefit is without an increase in side effects.
• Identify three pre-existing conditions / characteristics or pre-existing therapies, which can result in poor postoperative pain control and potentially lead to chronic pain
  – A. Prior Opioid Tolerance
  – B. Buprenorphine treatment prior to surgery
  – C. Naltrexone treatment prior to surgery
  – D. Congestive Heart Failure
  – E. A, B, and C

• Assess why and how to prevent or minimize the impact on postoperative pain management. Buprenorphine treatment prior to ELECTIVE surgery
  – A. Planned surgery may result in moderate to severe pain and patient taking greater than 8mg of Buprenorphine. Stop Buprenorphine 72 hours prior to surgery
  – B. Planned surgery may result in minimal to no pain and patient still taking Buprenorphine. Continue Buprenorphine and do not change the Buprenorphine dose. Also consider adjuncts such as NSAIDs, acetaminophen, local anesthetics, or regional anesthetics techniques.
  – C. Planned surgery may result in moderate to severe pain and patient has been off Buprenorphine. Plan for the patient may display high opioid tolerance and consider adjuncts such as NSAIDs, acetaminophen, local anesthetics, or regional anesthetic techniques
  – D. All of the above

What is Enhanced Recovery After Surgery (ERAS)

Enhanced recovery after surgery (ERAS) protocols: Time to change practice?
Megan Malinik, MSc, MD; Rowan G. Casey, MBChB, MD, FRCS(Urol); Peter Black, MD, FRCSc, FACS; Anthony J. Kaukonis, MBChB MD FRCS(Urol)

Can Urol Assoc J 2011;5 (5): 342-8;DOI:10.5489/cuaj.11002

• “Initiated by Professor Henrik Kehlet in the 1990s, ERAS, enhanced recovery programs (ERPs) or “fast-track” programs have become an important focus of perioperative management after colorectal surgery, vascular surgery, thoracic surgery and more recently radical cystectomy.”

• The goal is to attempt to modify the physiologic and psychological responses to major surgery.
  – Reduction in complications
  – Reduction in length of stay
  – Improvements in cardiopulmonary function
  – Earlier return of bowel function
  – Earlier resumption of normal activities
What is Enhanced Recovery After Surgery (ERAS)

Enhanced recovery after surgery (ERAS) protocols: Time to change practice?

Megan Melnyk, MSc, MD; Rowan G. Casey, MBChB, MD, FRCS(Urol); Peter Black, MD, FRCSC, FACS;
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Can Urol Assoc J 2011; 5(5): 342-8; DOI:10.5489/cuaj.11002

Key principles of ERAS protocol

- Preoperative counseling
- Preoperative nutrition
  - Avoidance of perioperative fasting
  - Carbohydrate loading up to 2 hours preoperatively
- Standardized anesthetic (epidural) and analgesic (non-opioid) regimens
- Early mobilization
Enhanced Recovery After Surgery
A Review

Olle Ljungqvist, MD, PhD, Michael Scott, MD, Kenneth C. Fearon, MD, PhD

IMPORTANCE Enhanced Recovery After Surgery (ERAS) is a paradigm shift in perioperative care, resulting in substantial improvements in clinical outcomes and cost savings.

OBSERVATIONS Enhanced Recovery After Surgery is a multidisciplinary approach to the care of the surgical patient. Enhanced Recovery After Surgery process implementation involves a team consisting of surgeons, anesthetists, an ERAS coordinator (often a nurse or a physician assistant), and staff from units that care for the surgical patient. The care protocol is based on published evidence. The ERAS Society, an international nonprofit professional society that promotes, develops, and implements ERAS programs, publishes updated guidelines for many operations, such as evidence-based modern care changes from overnight fasting to carbohydrate drinks 2 hours before surgery, minimal invasive approaches instead of large incisions, management of fluids to seek balance rather than large volumes of intravenous fluids, avoidance of or early removal of drains and tubes, early mobilization, and serving of drinks and food the day of the operation. Enhanced Recovery After Surgery protocols have resulted in shorter length of hospital stay by 20% to 30% and similar reductions in complications, while readmissions and costs are reduced. The elements of the protocol reduce the stress of the operation to retain anabolic homeostasis. The ERAS Society conducts structured implementation programs that are currently in use in more than 20 countries. Local ERAS teams from hospitals are trained to implement ERAS processes. Audit of process compliance and patient outcomes are important features. Enhanced Recovery After Surgery started mainly with colorectal surgery but has been shown to improve outcomes in almost all major surgical specialties.

CONCLUSIONS AND RELEVANCE Enhanced Recovery After Surgery is an evidence-based care improvement process for surgical patients. Implementation of ERAS programs results in major improvements in clinical outcomes and cost, making ERAS an important example of value-based care applied to surgery.

Published online January 11, 2017.

Table 2. ERAS Society Guideline Elements for Colonic Resections

<table>
<thead>
<tr>
<th>Element</th>
<th>Target Effect and/or Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preadmission</td>
<td>Reduction of smoking and excessive intake of alcohol</td>
</tr>
<tr>
<td>Preoperative nutritional screening and, as needed, assessment and nutritional support</td>
<td>Reduce complications</td>
</tr>
<tr>
<td>Medical optimization of chronic disease</td>
<td>Reduce complications</td>
</tr>
<tr>
<td>Preoperative structured preoperative information and engagement of the patient and relatives or caretakers</td>
<td>Reduce anxiety, involve the patient to improve compliance with protocol</td>
</tr>
<tr>
<td>Preoperative carbohydrate treatment</td>
<td>Reduce insulin resistance, improve well-being, possibly faster recovery</td>
</tr>
<tr>
<td>Preoperative prophylaxis against thrombosis</td>
<td>Reduce thromboembolic complications</td>
</tr>
<tr>
<td>Preoperative prophylaxis against infection</td>
<td>Reduce infection rates</td>
</tr>
<tr>
<td>Prophylaxis against nausea and vomiting</td>
<td>Minimize postoperative nausea and vomiting</td>
</tr>
<tr>
<td>Intraoperative minimal invasive surgical techniques</td>
<td>Reduce complications, faster recovery, reduce pain</td>
</tr>
<tr>
<td>Standardized anesthesia, avoiding long-acting opioids</td>
<td>Avoid or reduce postoperative ileus</td>
</tr>
<tr>
<td>Maintaining fluid balance to avoid over- or underhydration, administer vasopressors to support blood pressure control</td>
<td>Reduce complications, reduce postoperative ileus</td>
</tr>
<tr>
<td>Epidural anesthesia for open surgery</td>
<td>Reduce stress response and insulin resistance, basic postoperative pain management</td>
</tr>
<tr>
<td>Restrictive use of surgical site drains</td>
<td>Support mobilization, reduce pain and discomfort, no proven benefit of use</td>
</tr>
<tr>
<td>Removal of nasogastric tubes before reversal of anesthesia</td>
<td>Reduce the risk of pneumonia, support oral intake of solids</td>
</tr>
<tr>
<td>Control of body temperature using warm air flow blankets and warmed intravenous infusions</td>
<td>Reduce complications</td>
</tr>
<tr>
<td>Postoperative early mobilization (day of surgery)</td>
<td>Support return to normal movement</td>
</tr>
<tr>
<td>Early removal of urinary catheters and intravenous fluids (morning after surgery)</td>
<td>Support ambulation and mobilization</td>
</tr>
<tr>
<td>Use of chewing gums and laxatives and peripheral opioid-blocking agents (when using opioids)</td>
<td>Support return of gut function</td>
</tr>
<tr>
<td>Total parenteral nutrition (if nil by mouth for more than 3 days)</td>
<td>Increase energy and protein intake in addition to normal food</td>
</tr>
<tr>
<td>Multimodal approach to opioid sparing pain control</td>
<td>Pain control reduces insulin resistance, supports mobilization</td>
</tr>
<tr>
<td>Multimodal approach to control of nausea and vomiting</td>
<td>Minimize postoperative nausea and vomiting and support energy and protein intake</td>
</tr>
<tr>
<td>Prepare for early discharge</td>
<td>Avoid unnecessary delays in discharge</td>
</tr>
</tbody>
</table>

Audit of outcomes and process in a multiprofessional, multidisciplinary team on a regular basis | CONTROL OF PRACTICE (A KEY TO IMPROVE OUTCOMES) |


* For details and references, see the guidelines at http://www.erasociety.org.
• The key principles of the Enhanced Recovery after Surgery protocol that lead to a reduction in complications or essentially improve clinical outcomes along with decreased hospital stay and reduced costs?
  – A. Early mobilization (day of surgery)
  – B. Multimodal approach to opioid-sparing pain control
  – C. Early removal of urinary catheters and intravenous fluids (morning after surgery)
  – D. Preoperative prophylaxis against thrombosis
  – E. Minimally invasive surgical techniques
  – F. Standardized anesthesia, avoiding long-acting opioids
  – G. ALL OF THE ABOVE

Enhanced Recovery After Surgery (ERAS) for gastrointestinal surgery, part 2: consensus statement for anaesthesia practice

ActaAnaesthesiologica Scandinavica 60 (2016) 289–334

• Pre-anesthetic medications
  – Summary and recommendation: long-acting anxiolytic and opioids should be avoided as they may delay discharge. Short-acting benzodiazepine should be avoided in the elderly.
    • Patients planning major surgery are commonly anxious. Anxiety has been shown in many studies the most common predictor for postoperative pain and pain intensity
    • Preoperative assessment – address preoperative analgesics and anxiolytic medications along with education.
    • “Targeted use of short-acting anxiolytics and analgesics to facilitate regional anesthetic procedures and insertion of intravascular lines at adequate doses based on age and comorbidities.”
    • Avoid short-acting benzodiazepines in older patients (age > 60)
    • Long-acting sedatives and opioids should be avoided as they may impair mobilization
**Multimodal Analgesia (MMA)**

- Open Abdominal Surgery
  - Thoracic Epidural Analgesia – Strong for using it
  - IV Lidocaine Infusion (IVLI) – Moderate for using it
  - Continuous Wound Infusion – Weak for using it
  - Transversus Abdominis Plane (TAP) blocks – Moderate for using it
- Laparoscopic Abdominal Surgery
  - Thoracic Epidural Analgesia – Weak for using it
  - IV Lidocaine Infusion (IVLI) – Moderate for using it
  - Intrathecal Morphine – Moderate for using it
  - Transversus Abdominis Plane (TAP) Blocks – Moderate for using it

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**TAP Blocks**

*Figure 1. Cutaneous innervation of the abdominal wall. Coloured region is mostly blocked by a single injection posterior TAP block.*

NEW YORK SCHOOL OF REGIONAL ANESTHESIA (WWW.NYSORA.COM)
**Multimodal Analgesia (MMA)**

- MMA regimen based on routine use of NSAIDs, COX-2 and acetaminophen if not contraindicated for open and laparoscopic abdominal procedures to reduce opioid exposure and dose-dependent side effects thus impairing recovering

- NSAIDs and COX-2 inhibitors (short term use)
  - Improve postoperative analgesia
  - Reduce opioid consumption and side effects by up to 30%
  - Concerns regarding cardiovascular risk and bone healing

- Acetaminophen has shown to improve postoperative analgesia, have an opioid sparing effect, but not reduce opioids side effects.

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**NSAID Risk Assessment for Long Term Treatment**

[Diagram showing the assessment process]

### NSAIDs – Propionic Acids

<table>
<thead>
<tr>
<th>Drug Name (Brand)</th>
<th>Routes</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fenoprofen (Nalfon)</td>
<td>PO</td>
<td>200 mg q4-6h prn mild to moderate pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>400- 600 mg 3-4 times daily (OA / RA)</td>
</tr>
<tr>
<td>Flubiprofen (Ansaid)</td>
<td>PO</td>
<td>50 mg q6-8h prn OA/RA (max daily 300mg)</td>
</tr>
<tr>
<td>Ibuprofen (Motrin, Advil)</td>
<td>PO IVPB(55)</td>
<td>400 –600 mg q6h or 800 mg q8h (pain)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>800mg q6h (inflammation)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>400 – 800mg (over 30 min) q6h prn (must be well hydrated)</td>
</tr>
<tr>
<td>Ketoprofen (Orudis, Ourvail)</td>
<td>PO PO ER</td>
<td>50mg QID or 75mg TID max daily 300mg (OA / RA)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>200mg QD</td>
</tr>
<tr>
<td>Naproxen (Naprosyn)</td>
<td>PO PO DR</td>
<td>500 – 1000 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>750 – 1000 mg daily (OA / RA)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>500 mg q12h or 250mg q6-8h (pain)</td>
</tr>
<tr>
<td>Naproxen Sodium (Aleve, Anaprox)</td>
<td>PO PO ER</td>
<td>220 mg (550 mg) sodium = 200 mg (500 mg) base</td>
</tr>
<tr>
<td></td>
<td></td>
<td>See above dosing</td>
</tr>
<tr>
<td>Oxaprozin (Daypro)</td>
<td>PO</td>
<td>600 mg -1200 mg QD (OA / RA)</td>
</tr>
</tbody>
</table>


### NSAIDs – Phenylacetic Acids

<table>
<thead>
<tr>
<th>Drug Name (Brand)</th>
<th>Routes</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diclofenac Acid (Zorvelex)</td>
<td>PO</td>
<td>18-35 mg TID (Pain)</td>
</tr>
<tr>
<td>Diclofenac Potassium (Cataflam, Cambia)</td>
<td>PO PO PKT</td>
<td>25 mg capsule QID or 50mg tablet TID (Pain)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50 mg 2-3 x day (OA) or 50 mg 3-4 x day (RA)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50 mg or 1 pkt in 1-2 oz water x1dose (migraine)</td>
</tr>
<tr>
<td>Diclofenac Sodium (Voltarin, Voltarin XR, Voltarin 1% Gel, Dyloject)</td>
<td>EC DR PO DR Topical Gel IV (SSS)</td>
<td>50 mg 2-3 x day (OA), 50 mg 3-4 x day (RA)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>100mg daily (OA or RA) dose may be increased to BID (max)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 gm QID lower extremity, 2 gm QID upper extremity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>37.5 mg over 15 seconds q6h prn (pain)</td>
</tr>
<tr>
<td>Diclofenac Epolamine (Flector)</td>
<td>Topical</td>
<td>1 patch BID (to most painful site)</td>
</tr>
<tr>
<td>Diclofenac Sodium + Misoprostil (Arthrotec)</td>
<td>PO</td>
<td>1 tablet TID (OA)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 tablet TID – QID (RA)</td>
</tr>
</tbody>
</table>

**NSAIDs – Carbo & Heterocyclic Acids**

<table>
<thead>
<tr>
<th>Drug Name (Brand)</th>
<th>Routes</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indomethacin (Indocin,</td>
<td>PO</td>
<td>25 mg BID to TID, inc daily by 25-50mg at weekly intervals</td>
</tr>
<tr>
<td>Tivorbex)</td>
<td>PO (Tivorbex)</td>
<td>to a max daily dose of 150 mg to 200 mg</td>
</tr>
<tr>
<td></td>
<td>PO ER</td>
<td>20 mg TID or 40mg BID or TID</td>
</tr>
<tr>
<td></td>
<td>Supp</td>
<td>75 mg QD, may increase to BID if tolerated</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50 mg BID to TID</td>
</tr>
<tr>
<td>Ketorolac (Toradol)</td>
<td>PO</td>
<td>(&lt;65 years &amp; &gt; / = 50kg) 20 mg LD then 10mg q4-6 hrs prn max 40mg / day</td>
</tr>
<tr>
<td></td>
<td>IV ($)</td>
<td>(&gt;65 year or &gt; &amp; &lt; 50kg) 10 mg q4-6 hrs prn max 40mg / day</td>
</tr>
<tr>
<td></td>
<td>Nasal Spray</td>
<td>(&gt;65 year or &gt; &amp; &lt; 50kg) 30 mg (over 15 seconds) q6h max 120mg / day</td>
</tr>
<tr>
<td></td>
<td>(SSSSS)</td>
<td>(&gt;65 years &amp; &gt; / = 50kg) 15 mg (over 15 seconds) q6h max 60mg / day</td>
</tr>
<tr>
<td></td>
<td>15.75mg / spray</td>
<td>(&gt;65 years &amp; &gt; / = 50kg) 1 spray each nostril every 6-8 hr (NMT 4 doses/day)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(&lt;65 years or &gt; &lt; 50kg) 1 spray one nostril every 6-8 hr (NMT 4 doses/day)</td>
</tr>
<tr>
<td>Etodolac (Lodine)</td>
<td>PO</td>
<td>400 mg to 1000 mg QD</td>
</tr>
<tr>
<td></td>
<td>PO ER</td>
<td>200 – 300 mg 2-3 x day (pain)</td>
</tr>
<tr>
<td>Sulindac (Clinoril)</td>
<td>PO</td>
<td>150 mg BID (OA or RA) Max 400 mg per day</td>
</tr>
<tr>
<td></td>
<td></td>
<td>200mg BID for 7-14 days (pain)</td>
</tr>
<tr>
<td>Tolmentin (Tolectin)</td>
<td>PO</td>
<td>Initiate 400 mg TID, adjust after 1-2 wks adjust to maintenance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>200 – 600 mg TID</td>
</tr>
</tbody>
</table>

Levi comp 2016


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**NSAIDs - Other**

<table>
<thead>
<tr>
<th>Drug Name (Brand)</th>
<th>Routes</th>
<th>Dose</th>
<th>Chemical Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin (Ecotrin)</td>
<td></td>
<td>325 – 1000 mg q4-6 hrs prn (NMT 4 gm / 24 hrs)</td>
<td>Salicylic Acids</td>
</tr>
<tr>
<td>Diffunisal (Dolobid)</td>
<td>PO</td>
<td>250 – 500 mg BID, max 1500 mg / day</td>
<td>Salicylic Acids</td>
</tr>
<tr>
<td>Meloxicam (Mobic tab,</td>
<td>PO tab</td>
<td>7.5 mg QD, max 15mg QD (OA or RA)</td>
<td>Oxicam (non-selective COX-2)</td>
</tr>
<tr>
<td>Vivlodex capsule)</td>
<td>PO cap</td>
<td>5 mg QD, max 10mg QD (OA)</td>
<td></td>
</tr>
<tr>
<td>Piroxicam (Feldene)</td>
<td>PO</td>
<td>20 mg QD</td>
<td>Oxicam</td>
</tr>
<tr>
<td>Nambumetone (Relafen)</td>
<td>PO</td>
<td>1000 mg QD (max dose 1000 mg BID)</td>
<td>Non-Acetic Acids</td>
</tr>
<tr>
<td>Celecoxib (Celebrex)</td>
<td>PO</td>
<td>100mg BID or 200 mg QD (OA)</td>
<td>Selective COX-2 Inhibitor</td>
</tr>
<tr>
<td></td>
<td></td>
<td>100 – 200 mg BID (RA)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>400 mg Post-procedure (acute pain)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>400mg loading dose then 200 mg BID (acute pain)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>800 mg loading dose then 400 mg q12h (acute gout)</td>
<td></td>
</tr>
</tbody>
</table>
Cyclooxygenases: new forms, new inhibitors, and lessons from the clinic

TIMOTHY D. WARNER*2 AND JANE A. MITCHELL*2

The William Harvey Research Institute, Barts and the London, Queen Mary's School of Medicine and Dentistry, Charterhouse Square, London, U.K. and *Unit of Critical Care Medicine, Royal Brompton Hospital, Imperial College School of Medicine, London, U.K.

Increasing COX-1 selectivity

Increasing COX-2 selectivity

Relative Selectivity of NSAIDs as Inhibitors of COX-1 and COX-2 by Chemical Class

<table>
<thead>
<tr>
<th>Chemical Class</th>
<th>COX-1 Selectivity</th>
<th>COX-2 Selectivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propionic Acids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carboxy-heterocyclic Acids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oralkms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phenylacetic Acids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COX-2 Selective Inhibitors</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Available as IV formulation in US


Federation of American Societies for Experimental Biology


Richard Wheeler Pharm D, BCPs
10.2015
- Distinguish between the three parenteral NSAIDs manufactured in the United States.
- Identify which are administered IV push versus which are administered by IVPB or intermittent infusion
  - A. Injectable Ketorolac and Ibuprofen can be administered by IV push while Diclofenac requires dilution and administration by intermittent infusion or IVPB.
  - B. Injectable Ketorolac can be administered by IV push while Ibuprofen and Diclofenac requires dilution and administration by intermittent infusion or IVPB.
  - C. Injectable Ketorolac and Diclofenac can be administered by IV push while ibuprofen requires dilution and administration by intermittent infusion or IVP.
  - D. Parecoxib 40mg is diluted with 2ml of NS and administered IV injection. Ketorolac IV is administered IV over 15 seconds while Ibuprofen is administered by intermittent infusion or IVPB.

FDA strengthens warning that non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs) can cause heart attacks or strokes

July 2015 - FDA is recommending drug makers update the labels for all non-aspirin NSAIDs to include the following information:

- “The risk of heart attack or stroke can occur as early as the first weeks of using an NSAID. The risk may increase with longer use of the NSAID.”
- “The risk appears greater at higher doses.”
- “It was previously thought that all NSAIDs may have a similar risk. Newer information makes it less clear that the risk for heart attack or stroke is similar for all NSAIDs; however, this newer information is not sufficient for us to determine that the risk of any particular NSAID is definitely higher or lower than that of any other particular NSAID.”

http://www.fda.gov/Drugs/DrugSafety/ucm451800.htm
"NSAIDs can increase the risk of heart attack or stroke in patients with or without heart disease or risk factors for heart disease. A large number of studies support this finding, with varying estimates of how much the risk is increased, depending on the drugs and the doses studied."

"In general, patients with heart disease or risk factors for it have a greater likelihood of heart attack or stroke following NSAID use than patients without these risk factors because they have a higher risk at baseline."

"Patients treated with NSAIDs following a first heart attack were more likely to die in the first year after the heart attack compared to patients who were not treated with NSAIDs after their first heart attack."

"There is an increased risk of heart failure with NSAID use."

http://www.fda.gov/Drugs/DrugSafety/ucm451800.htm

### Table 2. Studies Addressing Optimal Dose

<table>
<thead>
<tr>
<th>Authors</th>
<th>N</th>
<th>Surgery</th>
<th>Design</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Khan et al.</td>
<td>175</td>
<td>Laminectomy</td>
<td>Placebo, 600 mg, 900 mg, or 1,200 mg of gabapentin given preoperatively or postincision</td>
<td>Patients receiving either 900 or 1,200 mg had lower pain scores during the first 24 h compared with the 600 mg and placebo groups</td>
</tr>
<tr>
<td>Pandey et al.</td>
<td>100</td>
<td>Discectomy</td>
<td>Placebo, 300 mg, 600 mg, 900 mg, or 1,200 mg of gabapentin given 2 h preoperatively</td>
<td>Patients receiving ≥600 mg had lower visual analog scores at all time points compared with placebo or 300 mg groups</td>
</tr>
<tr>
<td>Van Elstraete et al.</td>
<td>67</td>
<td>Lumbar spinal fusion</td>
<td>Determination of optimal gabapentin dose for 30% reduction in morphine use by an up-and-down sequential allocation technique</td>
<td>Optimal dose for 30–50% reduction in morphine use calculated at 21.7 mg/kg (1,500 mg per 70 kg)</td>
</tr>
<tr>
<td>Kim et al.</td>
<td>84</td>
<td>Lumbar spinal fusion</td>
<td>Placebo, 75 mg, or 150 mg of pregabalin preoperatively</td>
<td>Patients-controlled analgesia and adjuvant analgesic use were lower in the 150 mg group but not in the 75 mg group compared with placebo</td>
</tr>
<tr>
<td>Jokeia et al.</td>
<td>90</td>
<td>Laporoscopic gynecological surgery</td>
<td>Active placebo, 75 mg of pregabalin, or 150 mg of pregabalin preoperatively</td>
<td>Pain scores at rest and in motion were lower in the 150 mg group but not the 75 mg group compared with placebo</td>
</tr>
</tbody>
</table>
Perioperative Gabapentinoids
Choice of Agent, Dose, Timing, and Effects on Chronic Postsurgical Pain
Anesthesiology, V 119 • No 5
November 2013

- “It should now be generally accepted that the Gabapentinoids are effective in reducing immediate postoperative pain and opioid consumption.”
- “the existing studies suggest that higher preoperative doses and additional postoperative doses are advantageous in reducing immediate postsurgical pain.”
- “we believe the current evidence is sufficient to recommend that either Gabapentin 1,200 mg or Pregabalin 300mg should be given at least 2h before surgery for patients at risk of developing either severe acute pain (e.g., the chronic opioid-consuming patient) or prolonged pain after surgery (e.g., thoracotomy).”

- “The positive outcomes reported by Buvanendran suggest that continued dosing of Gabapentinoids for 14 days after surgery is warranted. We recommend either postoperative Gabapentin 600 mg thrice a day or Pregabalin 150 mg twice a day.”
- “Postoperative Gabapentinoids dosage should be decreased or stopped in the face of sedation, dizziness, or confusion.”
- “Given the evidence suggesting that it takes 8 hr for Pregabalin to reach peak cerebrospinal fluid levels (and possibly 4–6 hr for Gabapentin to reach peak cerebrospinal fluid levels), it is possible that starting dosing the night before surgery may ultimately prove more beneficial than initiating dosing 2 h before surgery, but this effect may be at the risk of inducing dizziness, sedation, or confusion at home before surgery.”
Reported benefits of perioperative Lidocaine infusion in an Enhanced Recovery After Surgery (ERAS) program
- Reduction in
  - Pain
  - Nausea
  - Ileus duration
  - Opioid requirement
  - Length of hospital stay
- “These effects are observed with infusion rates of intravenous Lidocaine that mimics plasma Lidocaine concentrations obtained during epidural administration (approximately 1 μM).”
- The clinical effects in the majority of the trials exceeded the duration of the infusion by more than 8.5 hours, which is over 5 times the half-life of Lidocaine.

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![Figure 2. Representative protocol for use of intravenous Lidocaine for perioperative analgesia. APS = acute pain service, PACU = postanesthesia care unit; POD = postoperative day. Adapted from University of Virginia Enhanced Recovery After Surgery (ERAS) Protocol for Colorectal Surgery.](image-url)
Continuous infusion of perioperative lidocaine has a clear advantage in patients undergoing abdominal surgery as it provides significant pain relief, reduces postoperative opioid consumption, decreases opioid-induced nausea and vomiting, and promotes faster return of bowel function, allowing for a shorter hospital stay. However, these benefits were not demonstrated in patients undergoing total hip arthroplasty, cardiac surgery or tonsillectomy. Further studies are needed to assess the efficacy of intravenous lidocaine in other surgical populations.
**Perioperative intravenous glucocorticoids can decrease postoperative nausea and vomiting and pain in total joint arthroplasty**

A meta-analysis and trial sequence analysis


**Abstract**

**Background:** This meta-analysis aimed to demonstrate the efficacy and safety of intravenous glucocorticoids for reducing pain intensity and postoperative nausea and vomiting (PONV) in patients undergoing total joint arthroplasty (TJA).

**Methods:** PubMed, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, and Google databases were searched for randomized controlled trials (RCTs) comparing intravenous glucocorticoids versus no intravenous glucocorticoids or sham for patients undergoing TJA. Outcomes included visual analogue scale (VAS) pain at 12, 24, and 48 hours; the occurrence of PONV; length of hospital stay; the occurrence of infection; and blood glucose levels after surgery. We calculated risk ratios (RR) with a 95% confidence interval (CI) for dichotomous outcomes and the weighted mean difference (WMD) with a 95% CI for continuous outcomes. Trial sequential analysis was also used to verify the pooled results.

**Results:** Thirteen clinical trials involving 21 patients were ultimately included in this meta-analysis. The pooled results indicated that intravenous steroids can decrease VAS at 12 hours (WMD = −8.54, 95% CI: −11.55 to −5.53, P = 0.000; I² = 35.1%), 24 hours (WMD = −7.48, 95% CI: −13.36 to −1.60, P = 0.013; I² = 91.8%), and 48 hours (WMD = −1.90, 95% CI: −3.75 to −0.05, P = 0.044; I² = 84.5%). Intravenous steroids can decrease the occurrence of PONV (RR = 0.56, 95% CI: 0.44−0.73, P = 0.000; I² = 33.1%). There was no significant difference in the length of hospital stay, incidence of infection, and blood glucose levels after surgery.

**Conclusion:** Intravenous glucocorticoids not only alleviate early pain intensity but also decrease PONV after TJA. More high-quality RCTs are required to determine the safety of glucocorticoids before making final recommendations.

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**Perioperative Single Dose Systemic Dexamethasone for Postoperative Pain**

**A Meta-analysis of Randomized Controlled Trials**

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**Background:** Dexamethasone is frequently administered in the perioperative period to reduce postoperative nausea and vomiting. In contrast, the analgesic effects of dexamethasone are not well defined. The authors performed a meta-analysis to evaluate the dose-dependent analgesic effects of perioperative dexamethasone.

**Methods:** We followed the PRISMA statement guidelines. A wide search was performed to identify randomized controlled trials that evaluated the effects of a single dose systemic dexamethasone on postoperative pain and opioid consumption. Meta-analysis was performed using a random-effect model. Effects of dexamethasone dose were evaluated by pooling studies into three dosage groups: low (less than 0.1 mg/kg), intermediate (0.11−0.2 mg/kg) and high (≥0.21 mg/kg).

**Results:** Twenty-four randomized clinical trials with 2,751 subjects were included. The mean (95% CI) combined effects favored dexamethasone over placebo for pain at rest (≤4 h, 0.32 [0.47 to −0.18], 24 h, −0.49 [−0.67 to −0.31]) and with movement (≤4 h, −0.64 [−0.86 to −0.41], 24 h, −0.47 [−0.71 to −0.24]). Opioid consumption was decreased to a similar extent with moderate −0.82 (−1.30 to −0.42) and high −0.85 (−1.24 to −0.46) dexamethasone, but not decreased with low-dose dexamethasone −0.18 (−0.39−0.03). No increase in analgesic effectiveness or reduction in opioid use could be demonstrated between the high- and intermediate-dose dexamethasone. Preoperative administration of dexamethasone appears to produce a more consistent analgesic effect compared with intraoperative administration.

**Conclusion:** Dexamethasone at doses more than 0.1 mg/kg is an effective adjunct in multimodal strategies to reduce postoperative pain and opioid consumption after surgery. The preoperative administration of the drug produces less variation of effects on pain outcomes.
Intraoperative Ketamine Reduces Perioperative Opiate Consumption in Opiate-dependent Patients with Chronic Back Pain Undergoing Back Surgery

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- **Background:** Ketamine is an N-methyl-D-aspartate receptor antagonist that has been shown to be useful in the reduction of acute postoperative pain and analgesic consumption in a variety of surgical interventions with variable routes of administration. Little is known regarding its efficacy in opiate-dependent patients with a history of chronic pain.
- **Results:** Total morphine consumption (morphine equivalents) was significantly reduced in the treatment group 48 hr after the procedure. It was also reduced at 24 hr and at 6 weeks. The average reported pain intensity was significantly reduced in the postanesthesia care unit and at 6 weeks. The groups had no differences in known Ketamine or opiate related side effects.
- **Conclusions:** Intraoperative Ketamine reduces opiate consumption in the 48-h postoperative period in opiate dependent patients with chronic pain. Ketamine may also reduce opioid consumption and pain intensity throughout the postoperative period in this patient population. This benefit is without an increase in side effects.

- Distinguish three ERAS elements where pharmacy can have an impact to improve patient postoperative care
  - A. Safely maximize adjunctive therapy to minimize opioid utilization
  - B. Educate surgeons and anesthesiologists options for Ketamine delivery for safe administration of subanesthetic doses for the opioid tolerant surgical patient.
  - C. Consult with surgeons and anesthesiologist to safely administer Lidocaine IV infusions for their open abdominal surgical patients safely for both intraoperative and postoperative settings with proper monitoring and nursing education on the med/surgical floor.
  - D. All of the above
ALTHERNATIVES IN PAIN MANAGEMENT

REVIEW OF DRUGS/PHARMACOTHERAPY

A practical guide to tapering opioids

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Abstract

Tapering opioids is one of the most daunting dilemmas in clinical practice today. The decision to taper opioids is based on many factors, including a lack of efficacy, unacceptable risk, perioperative management, noncompliance, or patient preference. Tapering in the perioperative setting is quite common, though more complex in patients previously taking chronic opioid therapy. Outside of a medical emergency, opioid tapers are best managed in an outpatient setting, allowing for adjustments and more long-term nonopioid pain management, if necessary. No single strategy can be applied to all patients, and very few published guidelines are available for reference. Dose reductions and schedules are highly variable across available guidelines and literature. Dose reductions range from 10% to 50%, with a frequency ranging from daily reductions to every 2 weeks. Most guidelines address the concern of preventing physical withdrawal symptoms; however, few address the psychological ramifications of tapering. Individualized regimens and a willingness to adjust schedules and doses allow for improved patient comfort. The goal is to complete tapering without any symptoms of withdrawal; however, this is not always possible. Several available agents may help ameliorate these symptoms, including antihypertensives, antihistamines, antianemics, antidepressants, anticonvulsants, and antipsychotics. Opioid tapering is rarely easy but should be a manageable process.
Tapering Long-term Opioid Therapy in Chronic Noncancer Pain: Evidence and Recommendations for Everyday Practice

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TABLE 1. Criteria Identifying Patients in Whom Discontinuation of Long-term Opioid Therapy Should Be Considered (Combining Those Published by the Substance Abuse Mental Health Services Agency17 and by Fishman18)

1. Inability to achieve or maintain anticipated pain relief or functional improvement despite reasonable dose escalation
2. Intolerable adverse effects at the minimum dose that produces effective analgesia, with reasonable attempts at opioid rotation unsuccessful
3. Persistent nonadherence with patient treatment agreement
   This can include inappropriate use, failure to comply with monitoring (after excluding this failure is due to personal cost burden), selling prescription drugs, forging prescriptions, stealing or borrowing drugs, aggressive demand for opioids, injecting oral or topical opioids, unsanctioned use of opioids, unsanctioned dose escalation, concurrent use of illicit drugs, obtaining opioids from multiple prescribers and/or multiple pharmacies, recurring emergency department visits for chronic pain management
4. Deterioration in physical, emotional, or social functioning attributed to opioid therapy
5. Resolution or healing of the painful condition

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• **Standard PC.01.02.07**
  – The hospital assesses and manages the patient’s pain and minimizes the risks associated with treatment.
  – The hospital involves patients in the pain management treatment planning process through the following:
    – Developing **realistic expectations** and measurable goals that are understood by the patient for the degree, duration, and reduction of pain
    – Discussing the objectives used to evaluate treatment progress (for example, **relief of pain** and improved **physical and psychosocial function**)
    – Providing education on pain management, treatment options, and safe use of opioid and non-opioid medications when prescribed
      (See also RI.01.02.01, EPs 6–8; RI.01.03.01, EP 6)
• **Standard PC.01.02.07**
  - The hospital reassesses and responds to the patient’s pain through the following:
    • Evaluation and documentation of response(s) to pain intervention(s) (See also RC.01.01.01, EP 7)
    • Progress toward pain management goals including **functional ability** (for example, ability to take a deep breath, turn in bed, walk with improved pain control)
    • Side effects of treatment
    • Risk factors for adverse events caused by the treatment

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**Accountability for Pain Relief: Use of Comfort-Function Goals**

*Chris Pasero, MS, RN*
*Margo McGaffery, MS, RN, FAAN*


- “A simple and effective method for building in accountability for pain relief and improving patient outcomes is to establish and use comfort-function goals with patients. Establishment of a **comfort-function goal** requires clinicians to describe to patients the essential activities of recovery and discuss the direct link between pain control and improved outcome.”
- “The comfort-function goal provides a tangible mechanism for evaluating the health care team’s performance in terms of relieving pain and improving patient outcomes.”
- “The preoperative teaching session provides the ideal opportunity to establish comfort-function goals with surgical patients.”
- “Many patients will need help in establishing realistic comfort-function goals.”
- “They can be **told to expect to feel pain**, but that it can likely be **reduced to a level** that will not prevent them from performing their recovery activities well.”
- “The comfort-function goal provides direction for both the patient and the clinician by establishing **expectations of care**.”
Questions