Managing Pain in the Peri-operative Period
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What’s your preference?

Pre-operative analgesia / sedation
Intra-operative analgesia
Post-operative analgesia / wellbeing
Day Surgery

What’s your preference?

Pre-operative analgesia / sedation
Intra-operative analgesia
Post-operative analgesia / wellbeing
Minimal Invasive Surgery – scopes, hernia, soft tissue surgery, etc.

What’s your preference?

Pre-operative analgesia / sedation
Intra-operative analgesia
Post-operative analgesia / wellbeing
Major Surgery e.g. abdominal, thoracic, etc.

Role of pre-operative Anaesthetic clinics?
Preferred post-operative analgesia?
Role of regional anaesthesia?
• nerve blocks
• spinal / epidural / plexus blocks
Organised acute Pain Service in your institution?
• nurse coordinated
• consultant rounds
• what’s important?
  • interventions techniques or structured delivery

Complexity of Pain
Physiology of Pain – Normal
→ Abnormal
Peri-operative Pain Management
• pre-operative
• operative
• post-operative
Take home message
General comments on opioids

General comments on opioids
Pain is what patient states it is!

Definition of pain (IASP)
An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.

Merskey 1979

Acute pain
Pain of recent onset and probable limited duration. Often an identifiable temporal and casual relationship to injury or disease. Ready & Edwards 92.

Chronic pain
Pain persists beyond the time of healing of injury and may not have an identifiable cause. Ready & Edwards 92.

Pain perception and pain pathways:
- Noxious stimuli affecting somatosensory system
- Protective mechanism that involves peripheral & central mechanisms
- Perception & experience of pain influenced by psychological and environmental factors of individuals (enormous variation)
- Local injury “neuropeptide/chemical soup” production. Commencement of peripheral and central sensitisation mechanism.

Four basic personality types
- Pain attitude & belief
- Psychological distress
- Illness behaviour
- Social environment

Contributing factors: PsychoSocial.

Complex BioPsychoSocial

Experience of pain often a composite of causes. Important to identify major component. Treatment/Management based upon this. Clinical decision.

Types of chronic (persistent) pain:
- Neuropathic pain
- Nociceptive pain (includes visceral & incident pain)
- Unexplained pain (psychogenic?)

Understanding basic pathophysiology of pain becomes an essential component in management.
Types of receptors
- mechano-receptors
- thermo-receptors
- chemical-receptors

Nerve fibres
- "C" fibre -- unmyelinated, heat, cold, mechanical
  chemical pain 0.5 – 1.5 µm 0.5 – 2 m/sec
  A-delta -- cold, mechanical, heat pain
  lightly myelinated  1 – 4 µm  12 – 30 m/sec
  A-beta -- myelinated, touch and pressure
  5 – 15 µm  30 – 70 m/sec
  A-gamma -- muscle spindle
  6 – 8 um myelinated  15 – 30 m/sec
  A-alpha -- primary muscle spindle, motor to skeletal muscle
  12 – 20 µm  70-120 m/sec

Peripheral sensitisation
- Tissue insult -- mast cells, lymphocytes, macrophages
- release inflammatory mediators
- syngangogenic inflammation
- sub. P, neurokinin A, CGRP
- sympathetic activation
- vasodilatation
- plasma protein release
  "chemical soup"
  i.e. K+, H+, serotonin, bradykinin, sub. P, histamine, 
  cytokines, NO, products of cyclo-oxygenase and 
  lipogenase pathways of arachidonic acid synthesising prostaglandins
- stimulates high threshold nociceptors
- peripheral sensitisation i.e. innocuous becomes noxious stimuli
- Antidromic & recruitment of non-nociceptive afferents.
- zone of 2° peripheral hyperalgesia / recruitment

Acute pain:
- stimulus ---- glutamate release
  + sensitises AMPA receptors + action pot.
  ---- Na. Chan. ---- EPSPs (excitatory post-synaptic potentials)

Result -- pain, C. Cortex
-- withdrawal

Acute pain experienced but no sensitisation with appropriate analgesia.

Spinal mechanism of inflam. pain:
- Neuropeptides -- Glutamate, Sub. P, CGRP.
  - Sub. P activates NK1 receptor (G-protein coupled receptor)
  - And CGRP most common neuropeptides and co-localised in 
    50 – 65% of nociceptive fibres.
  - SP -- generation of central sensitisation and hyperalgesia.
  - SP & CGRP decrease in concentration over a few days following 
    tissue injury and inflammation healing; but will increase if 
    the above continues. Hyperalgesia & allodynia result.

Where is Sub. P & glutamate manufactured?

Central sensitisation summary:
- NK-1 activation by SP
- AMPA activation by Glutamate
- non-NMDA receptor (metabotropic glutamate receptor) 
  activation by glutamate
- NMDA receptor sensitisation & VACC activation with 
  dislodgement of Mg plug. Na. & Ca. cascade and 
  phosphorylation activity.

Potential source of pre-emptive analgesia. (animal studies) 
  e.g. spinal block, etc.
  But only NMDA antagonists are effective.
Gate control theory

- Rubbing
- Microcyte activity
- Acupuncture

Acute pain
- Peripheral sensitisation
- Central sensitisation
- Sequence of events

IEG = immediate early genes; increase Protein synthesis.

Ref: Richard J. Traub 2004

NMDA receptor dorsal horn

Ca. cascade initiates NO activation and fos & Jun gene induction.

Neurolysis, nerve sprouting, neuroplasticity.

NEUROPLASTICITY & CENTRAL SENSITISATION

Lateral system --- Neospinothalamic tract
  (initial sharp, localised pain perception)

STT

Medial system --- Paleospinothalamic tract
  Brain stem
  Mid-brain
  Reticular formation
  Periaqueductal Gray area
  Limbic system
  Hypothalamus
  (slow, dull, prolonged, poorly localised)
  Activates sympathetic system

Limbic system
- Activates sympathetic system
- Periaqueductal Gray area
- Limbic system
- Hypothalamus
- slow, dull, prolonged, poorly localised

Mediation of pain perception

- Gate control theory
- Acute pain
- Neurolysis, nerve sprouting, neuroplasticity.

Neurolysis, nerve sprouting, neuroplasticity.

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**Thalamic projection**

Ventralis Postero-lateralis Nucleus input from dorsal column laminae III & IV (touch, vibration and pressure)

Neospinothalamic tract —— Sensory Cortex (sensory discrimination in pain perception)

Medial & Posterior Thalamic Nuclei input from Paleospinothalamic tract —— Sensory Cortex (Regulates emotional and unpleasant aspects of pain)

Activates Limbic system ± individual variation to pain perception and response

**Descending Pain Modulation / Inhibition**

3 pathways between mid-brain and dorsal horn

1. Raphe Magnus Nuclei
2. Nucleus Locus Cerulans of Pons
3. Nucleus Reticular Paragigantocellularis (Edinger-Westphal N.)

Activation —— release —— serotonin —— N-adrenalin —— cholecystokinin

Action at lamina III and IV

Activate PAG area —— rich in opioid receptors

—— release endogenous opioids —— exogenous opioid action

(Activation at lamina II —— inhibit “C” fibre)

**Ongoing acute pain, the following may take place: (summary)**

- Peripheral sensitisation
- Central sensitisation
- Suppression of inhibitory pathways — e. opioid, GABA cholecystokinin, NA, etc.
- Psychological / emotional input

**Managing post-operative pain should commence with pre-operative preparation.**

Psychological factors:

- Pre-operative anxiety, catastrophising neuroticism and depression are associated with higher pain intensity
- Pre-operative anxiety and depression are associated with an increased number of PCA demands and dissatisfaction with PCA (Linton 2002; Kalkman 2003; Palvin 2005; Ozalp 2003)

Education of patient and relevant staff (includes especially medical)

**Effective and successful post-operative pain management is dependant upon:**

(Education of medical, nursing, allied health and patients)

- Pre-operative education improves patient or carer knowledge of pain and encourages a more positive attitude towards pain relief (Shulham 1999; Hodgkinson 2000; Watkins 2001)
- Implementation of an effective acute pain service will improve pain relief and reduce incidence of side effects (Abour 2003; Endak 2004; Jones 2003)
- Staff education, use guidelines improves pain assessment, pain relief and prescribing practice. Standardised protocol is more important than individual techniques (ANZCA & FPM 2000; Pain Soc. 2003; ASA 2004)

**Incidence of chronic pain after surgery:**

(Further contributed by inadequate peri-operative Mx)

Type of surgery Incid. Chronic pain %

- Amputation 30 – 85
- Cholecystectomy 5 – 67
- Mastectomy 11 – 57
- Thoracotomy 3 – 56
- Vagotomy 0 – 52
- Vasectomy 0 – 30
- Vascular 0 – 42
- Dental surgery 0 – 13
- Hip 9 – 23
- Knee 5 – 25

(A. Pain Mx, ANZCA 2005)
Post-op. pain relief should consider:
- Effective post-operative pain relief to reasonable patient satisfaction
- Prevent post-surgical chronic/persistent pain

Risk factors for chronic post-surgical pain:
- Post-op. factors: Pain, moderate to severe, lasting more than 1 month
  - Repeat surgery
  - Psychological vulnerability
  - Workers compensation
- Intra-operative factors: Surgical approach with risk of nerve damage

What’s needed:
- Efficient Acute Pain Service (ANZCA acute pain Mx, 2005)
- Staff Education (ward staff, residents, all medical personnel, etc.)
- Surgeon’s understanding and participating essential
- Pre-operative Anaesthetic Clinic (LD Dorr. 2006)
- Appropriate education and organisational structures for delivery of pain relief rather than techniques (ANZCA acute pain Mx, 2005)

What’s our aim and objective?
- Satisfactory pain relief
- Patient to participate effectively to physical therapy/function
- Minimise secondary complications of pharmacotherapy
- Prevent or minimise incidence of chronic pain

Systemic analgesics:
- Paracetamol (Barden 2004)
- NSAIDs: Cox 1 & 2 (RCA 96; Lee 2001; Simmons 2003; Bottling 03)
- Nitrous oxide (Harding & Gibson 2000; Rosen 2002; Murat 2003)
- Ketamine (Carpenter & Dickensen 99; Hocking & Cousin 03)
- Antidepressants esp TCA (Collins 2000; Salero 2002; Tasmuth 2002)
- Anticonvulsants (Jensen 02; Mcquay 02)
- Membrane stabilisers (lignocaine, etc.) (Kaleo 98; Baranowski 99)
- Opioids (Yakhsh 76; Wang 79; Bernards 04)

Take-home message:
- Paracetamol & NSAIDs effective for acute pain (Cochran review)
- Paracetamol + NSAIDs improve analgesia (Cochran review)
- NSAID Tx and renal function
- COX-2 do not inhibit platelet function
- Short term COX-2 minimal gastric problem.
**Take home message:**

- N2O safe in labour and other acute pain states. (Rosen 2002)
- N2O neuropathy and bone marrow suppression rare (Riedel 99; Green 95)
- Ketamine opioid sparing effect. (Petrenko 2003; Sikiennik 95)
- Ketamine improves analgesic unresponsive to opioids. (Subramaniam 04)
- Ketamine useful – allodynia, hyperalgesia & opioid tolerant. (Weinbroum 03)

**Take home message:**

- TCA beneficial for neuropathic pain. (McQuay 99; Sindrup 99)
- Low doses in elderly
- Benefit in anxious/depressed pre-operative (TCA & SSRI’s). (Wallace 2002)
- Anticonvulsants for neuropathic pain. (Backonja 2002)
- Perioperative gabapentin & pregabalin reduces post-op pain and opioid requirement. (Cillis 2000; Bone 2002)

**Take home message:**

- Membrane stabilisers effective after nerve trauma/neuropathic pain (Koppert 2004; Kalso 98)
- Perioperative iv lignocaine reduces pain on movement & opioid requirement following major abdominal surgery. (Koppert 2004)
- Current evidence does not support cannabinoids in acute pain MX. (Campbell 2001; Buggy 2003)

**Take home message:**

- s/cut. or i/m opioids are as effective.
- Continuous iv infusion of opioid in general ward setting increased risk of respiratory depression compared to other methods. (6 fold) (Sichu 93)
- Transdermal fentanyl patch not recommended for acute pain. Titration problems, respiratory depression. (Sandfort 94; Grond 2000)
- Other than for severe acute pain, oral route choice for analgesia.
- Titration of opioid for severe pain best done by iv route. (Auburn 2001; MacIntyre 2001; Pang 2000)
- Rectal admin. Only if other routes are not possible. (Tramer 1998)

**Take home message:**

- Continuous lignocaine perineural infusion tolerance.
  Better with longer acting LA.
- CVS and CNS toxicity less severe with isomers Ropivacaine and Levo-bupivacaine then racemic Bupivacaine. (McLod 01; Scott 98)

**Take home message:**

- IT morphine produces better post-op analgesia than IT fentanyl after LSCS. (Dahil 1999)
- Opioid and LA opioidically synergistic. (Walker 2002)
- Morphine Viscdoule 24 hours pain relief. (Gupta 2001; Kelso 2003)
- No neurotoxicity from IT clin. Doses of morphine, fentanyl, sufentanyl. (Dahil 99; Cola 2000)
- Neuraxial IT opioid bolus dose: hydrophilic greater risk of delayed respiratory depression compared to lipophilic opioid. (Cousin & Mather 1984)
Take home message:

• IVI opioid provides better analgesia than conventional parenteral.
• Patients prefer PCA to conventional.
• IVI PCA does not reduce opioid consumption, hospital stay or lower incidence of opioid related adverse effects compared to conventional opioid admin. (Urquhart 88; White 90)
• Little evidence that one opioid is superior to another in PCA. (Sinatra 89; Stanley 98)
• S/cut PCA may be as effective as iv/ PCA. (Urquhart 88; White 90)
• Risk of respiratory depression increases with PCA and background infusion. (Notcutt 90; Fleming 92; Dal 2003)

Take home message:

• Adequate analgesia required prior to PCA commencement i.e. bolus doses.
• Routine anti-emetic not recommended in PCA
• Drug concentrations should be standardised within institutions to reduce program errors. (MacIntyre 2005)

Example of a case study in our institution and Future direction discussion

Our Institution: Hip & Knee prosthetic surgery. Intra-operative & post-operative management:

- Midazolam 1 – 5mg iv
- Fentanyl 100 – 500mcg iv
- Morphine 10 – 30mg iv (or im)
- Tramadol 100mg
- Ropivacaine 1mg

Combined spinal/epidural anaesthesia or only spinal
- Bupivacaine 0.5% 2 – 3.5mls + morphine 0.1 – 0.3mg
- Femoral or 3 in 1 nerve block

Immediate post-operative:

- PCA 700 – 1500mcg Fentanyl 12 – 36 hours (75 – 100mcg per hour)
- Morphine 40 – 100mg 30 – 36 hours
- PCA epidural at L3/4 Ropivacaine & Fentanyl (especially bilateral TKR)
- Pain Buster Ropivacaine 0.2% 135 mls with gentamicin (24 – 36 hours)

Additional post-operative medication may include the following:

- paracetamol
- tramadol
- diclofenac
- endone
- oxycontin
- hydromorphone
- lumiracoxib
- morphine im or s/cut (5 – 7 days)

Physiotherapy (active & passive)
Ambulation
Encouragement
Common secondary complications to pharmacotherapy: (especially opioids)

- nausea vomiting
- lethargy, drowsiness, lack of fluid intake, others
- drug induced hypotension
- ? Respiratory depression; ? Compromised healing
- ? Renal
- cognitive impairment

(many of the side effects and patient dissatisfaction due to opioid therapy)


Improving the above, better surgical outcome.

For hip and Knee prosthetic post-op care changed significantly last 5 years (series on 140 patients)
(AV Maheshwari et al, Cln Ortho; 2006)

Principle of multimodal therapy:

- different mechanism of action to produce analgesia
- attend to local wound effect
- spinal transmission
- thalamic/mid-brain influence
- cerebral cortex; patient education, expectations, minimise central sensitisation that magnifies pain.

(Dor et al, PA Saunders Elsevier; 2006: 1 - 4)

Newer multimodal analgesia technique

for total hip and knee arthroplasty

(Berger et al, 2005; AK Maheshwari et al, 2006)

Evolved over 5 years.

Changed surgical incisions, post-operative recovery, Anaesthesia and pain management.

More comfortable, less N/V, less lethargy;

This promotes active participation in early physical therapy and early discharge. This may prevent Rehabilitation admission.

Efficacy and side effects of analgesic therapy are major determinants of patient satisfaction.


Pre-medication:

(1 – 2 hours pre-op)

- anxiolytic e.g. midazolam, alprazolam, diazepam, etc.
- oral analgesic – oxycodone 10mg, paracetamol, others
- ? Anti-emic – maxidol, ondansetron, etc.
- ? prevent GIT irritation – proton pump inhibitor e.g. somac, lasec, etc.

Avoid parenteral opioid

Anaesthesia:

Epidural/spinal +/- GA

No opioids in epidural or intravenous

Sedation by infusion of Propofol 10mg/kg/hour

Laryngeal mask to maintain airway

Ondansetron 4mg of Metoclopramide 10mg intra-operative (prevent emesis)

Ropivicaine 10 (10mls) + morphine 4mg + steroid into joint (analgesia; prevents pri. Sensitisation by reducing inflammation)
Immediate post-operative:

- NSAID (Toradol 15 – 30mg imi) (renal function must be normal)
- Oxycodone
- Paracetamol

In general ward:

- oral NSAIDs e.g. Celecoxib, Lumiracoxib, etc. 7 – 21 days
- anti-emetic e.g. endapsertorn, metoclopramide
- Paracetamol 5 – 7 days
- oxycodone or oxycodine 3 – 5 days
- Aspire if high risk for DVT
- Close compression
- ambulate asap

Adverse effects

<table>
<thead>
<tr>
<th>Par. Opioids (%)</th>
<th>Multimodal Tx %</th>
</tr>
</thead>
<tbody>
<tr>
<td>(10 review studies)</td>
<td>(140 patients)</td>
</tr>
<tr>
<td>Po2</td>
<td>0 – 60</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>2 – 11</td>
</tr>
<tr>
<td>Hypotension</td>
<td>10 – 65</td>
</tr>
<tr>
<td>Ileus</td>
<td>0 – 25</td>
</tr>
<tr>
<td>Cognitive effect</td>
<td>6 – 23</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>0 – 79</td>
</tr>
<tr>
<td>Phthitus</td>
<td>10 – 74</td>
</tr>
<tr>
<td>Need for opioid antagonist</td>
<td>12.5</td>
</tr>
<tr>
<td>Nausea</td>
<td>11.1 – 76</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6.2 – 53</td>
</tr>
</tbody>
</table>

Authors conclusion:

1. Primary hip and knee surgeries successfully managed post-operatively by avoiding routine parenteral opioids.
2. Increased safety, reduced respiratory depression, drug induced hypotension, bradycardia, ileus are the greatest benefit to patients.
3. However, reduction of Nausea & vomiting provides the greatest patient satisfaction.

You are the leaders in your institution:

- organise effective pre-operative anaesthetic clinics
- appropriate standardised acute pain service
- consider psychological factors as important as peri-operative analgesia.
- side effects of pharmacotherapy delays recovery and patient dissatisfaction

Assoc. Prof. S. Raj Sundaraj

Natural opioids

- Morphine
- Codeine

Partial synthetic opioids

- Heroin
- Hydromorphone
- Buprenorphine
- Oxycodone (generic)
- Oxycodone SR

Synthetic opioids

- Fentanyl
- Sufentanil
- Pethidate
- Methadone
- Propoxyphene

Opioid tolerant patient

Definitions:

- Tolerance – a decrease in the effect of the drug over time.
- Physical Dependence – a physiological adaptation to a drug. Abrupt withdrawal leads to abstinence syndrome

Ref: Acute Pain Mx Scientific Evidence 2nd edition 2005 (NHMRC) & IASP conference 2005
Addiction — a disease characterised by aberrant drug seeking and drug taking behaviour. Craving, compulsive drug use, loss of control despite physical, social & psychological harm. Genetic factors may play a role.

Pseudo addiction — behaviour that may seem inappropriate drug seeking but are often of under treatment of pain and resolve when pain relief is inadequate.

Substance abuse disorder (SAD) — when the extent and pattern of substance use interfaces with the psychological and socio-cultural integrity of the person.

Pain is more strongly linked with emotion than any other area of perception. Martin 1988
Experience of pain is difficult to convey to others. Verillo 1975

Pain research has investigated every aspect of basic psychology course, including learning and motivation, psychophysics & perception, brain & behavior, memory & cognition, individual differences, development, personality, psychological disorders and social behavior. To truly understand a pain process holistically, one must understand physiology, psychology, sociology and spirituality. Craig & Reiman 1999


Thank you and have a nice day