Pain Management

Context

• Pain is defined as a subjective, unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage
• 1 in 5 experience moderate to severe pain
• Early acute pain interventions reduce incidence of chronic pain
• Acute pain is associated with tissue damage (nociceptive)
• Chronic pain may be associated with profound neurophysiological changes remote from the site of injury (neuropathic):
  ➢ New neurotransmitters
  ➢ Changes in neural connections
  ➢ Cortical reorganisation
• Models of chronic pain highlight the relationship between pain, thoughts, feelings and activities within a family and social context

How to measure pain

• Numerical Rating Scale (NRS)

  PAIN SCORE 0-10 NUMERICAL RATING

  0-10 Numerical Rating Scale

  0 No Pain
  1-5 Moderate Pain
  6-10 Severe Pain

• Visual Analogue Scale (VAS)

  No pain
  Worst pain ever

• Faces Rating Scale (FRS)
•Behavioural Rating Scale (BRS) for patients unable to self-report

The Analgesic Ladder

Step 1: Mild Pain (<3/10 on NRS)

Non-opioids

1) Aspirin
   • Irreversibly inactivates enzymes COX-1 (normal cells) and COX-2 (inflammatory cells) to reduce prostaglandin and thromboxane synthesis → effective analgesia and anti-inflammatory as well as anti-platelet aggregation effects to reduce thrombosis and cardiovascular risk (which is its preferred indication today)
   • Significant drug interactions with SSRIs, venlafaxine, warfarin and other anticoagulants → increased bleeding risk
   • Side effects include GI irritation, bleeding and ulcers, exacerbation of asthma, hypersensitive skin rash, Raye’s syndrome, salicylate poisoning in overdose (hyperventilation, vasodilatation, sweating)

2) Paracetamol
   • Inhibits COX enzymes (?COX-3) to reduce prostaglandin biosynthesis in the central nervous system but not in the peripheral tissues
   • Effective analgesic and antipyretic but minimal anti-inflammatory effect
   • Less irritant to the stomach so preferred in the elderly over aspirin
   • Side effects: suspected nephrotoxicity with long-term use, hepatotoxicity in overdose

3) Non-selective NSAIDS: ibuprofen, diclofenac, naproxen, indometacin, meloxicam, piroxicam
   • Reversibly inactivate COX-1 and COX-2 as well as possibly interfering with leukotriene formation by the lipoygenase pathway and G-protein mediated signal transduction → effective analgesic and significant anti-inflammatory effects
   • Particularly useful for chronic pain and inflammation e.g. OA, RA, back pain, bony metastases, also used for dysmenorrhoea, headache/migraine, dental pain, post-op pain
   • Significant drug interactions with SSRIs, venlafaxine, warfarin and other anticoagulants → bleeding, also reduce effects of other drugs e.g. diuretics and antihypertensives, potentiate ACEI nephrotoxicity
   • Contraindications include peptic ulceration, cardiovascular/stroke risk, heart failure, bleeding disorders, renal impairment, NSAID hypersensitivity, pregnancy and breast feeding (caution in the elderly)
   • Side effects include GI upset, irritation, bleeding and ulcers, exacerbation of asthma, hypersensitivity reactions, photosensitivity, renal failure, thrombosis, inhibition of bone healing, rarely hypertension

4) COX-2 Inhibitors: celecoxib, etoricoxib
   • Reversibly inactivate COX-2 only and therefore only inhibit prostaglandin synthesis by inflammatory cells → effective analgesic and anti-inflammatory action with fewer GI/systemic side effects
   • Licensed for relief of chronic inflammatory pain in OA, RA, AS, acute gout
   • Contraindications as above plus hypertension and oedema of any cause
   • Side effects as above with significantly reduced GI problems but significantly increased CV risk

5) Nefopam
   • Centrally acting non-opioid analgesic: appears to inhibit serotonin, dopamine and noradrenaline reuptake, as well as acting on histamine H3 receptors and glutamate
   • Cautions include hepatic/renal disease, elderly, urinary retention, epilepsy, pregnancy, breast feeding
   • Side effects include anticholinergic side effects, urinary retention, pink urine

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Step 2: Moderate Pain (3-6/10 on NRS)
Weak Opioids + Non-opioid +/- Adjuvants

1) Codeine preparations
   - 5-10% metabolised to morphine in vivo. Opiates are encephalin analogues which bind to specific opioid receptors in the CNS to induce analgesia:
     - µ1 receptors: supraspinal analgesia via pain nerve impulse blockade
     - µ2 receptors: respiratory depression, physical dependence
     - K receptors: sedation and spinal analgesia
   - Indicated for use in mild to moderate pain, diarrhoea and cough suppression
   - Preparations include cocodamol (paracetamol + codeine), codydramol (paracetamol + dihydrocodeine), codeine phosphate and dihydrocodeine \(\rightarrow\) oral, SC or IM administration
   - Caution in impaired respiratory function, asthma, hypotension, shock, bowel disorders, biliary tract disorders, convulsive disorders, prostatic hypertrophy, myasthenia gravis, elderly
   - Contraindications include acute respiratory depression, paralytic ileus (acute abdomen), raised ICP, head injuries (interfere with pupillary response assessment), comatose patients
   - Side effects of opiates include
     - Nausea, vomiting, constipation, dry mouth (\(\rightarrow\) O2 + ondansetron/cyclizine/one-off dose dexamethasone [centrally acting] + movicol/docucate [stool softeners])
     - Sedation, sleep disturbance, low mood, rarely psychosis
     - Biliary spasm
     - Large doses produce muscle rigidity, hypotension and respiratory depression
     - Long term use produces dependence and opiate withdrawal on cessation of treatment

2) NMDA receptor antagonists: tramadol, dextropropoxyphene (withdrawn)
   - Tramadol has an opioid effect and also enhances serotonergic and adrenergic pathways as well as antagonising NMDA receptors
   - Fewer opioid side effects e.g. respiratory depression, constipation, addiction
   - Cautions impaired consciousness, excessive bronchial secretions, opioid dependence
   - Contraindications epilepsy, acute porphyria
   - Side effects diarrhoea, fatigue, retching, gastritis, flatulence, hypertension, bronchospasm

Step 3: Severe Pain (>6/10 on NRS)
Strong Opioids + Non-Opioid +/- Adjuvants

1) Morphine
   - Oral: oromorph, MST (4hrs), MRT (12hrs), easy but all take up to an hour to peak efficacy
   - IV: slow/rapid infusion, patient controlled analgesia with syringe driver if sufficiently conscious
     - fast and effective, small doses, patient-tailored but expensive and increased infection risk
   - SC/IM: good for fast infrequent dosing but causes skin irritation and increased infection risk
   - Suppositories (if IV/oral not possible) and epidurals (less infections but invasive and ↑SE)
   - Hydromorphone: oral, SC/IM, IV; less nauseating than morphine, less hypotension

2) Methadone: oral, SC/IM; longer half life and less sedating

4) Oxycodone: oral, SC/IM, IV; used mainly in palliative care

5) Hydromorphone: oral; used in cancer

6) Fentanyl: oral or available transdermally as 72-hour patches for breakthrough pain

7) Buprenorphine: oral, sublingual, SC/IM, IV, patches; partial agonist, partially reversed by naloxone

8) Pethidine: oral, SC/IM, IV; prompt analgesia but short half life, used in obstetric pain

9) Others: diphenoxylate (diarrhoea), dipipanone, meptazinol (COPD), papaveretum, pentazocine

Adjuvant Analgesia: Neuropathic Pain

- Symptoms and signs of nerve pain include:
  - Unusual sensations e.g. burning/scalding, shooting/electric, stabbing, prickling, tingling, tight
  - Paraesthesia/numbness
  - Hyperalgesia (increased response to painful stimulus)
  - Allodynia (pain in response to normally non-painful stimulus)
  - Motor symptoms e.g. weakness, fasciculations, twitching
  - Increased sympathetic activity

- Possible drug treatments for neuropathic pain include
  - Tricyclic antidepressants: amitryptiline, imipramine, nortryptiline (help sleep/relaxation too)
  - Anticonvulsants: pregabalin, gabapentin, carbamazepine, lamotrigine
  - SNRIs: duloxetine, venlafaxine
  - SSRIs: not that good but paroxetine has modest efficacy
  - alpha-2 adrenergic agonists: clonidine, tinazidine
  - noradrenergics: buprenorphine

- Other treatments:
  - Tramadol is the best opioid analgesic for neuropathic pain
  - NICE Guidelines Care Pathway for neuropathic pain:
    - Offer oral amitryptiline 10mg/day or oral pregabalin 75mg twice a day
    - Try imipramine/nortryptiline if amitryptiline cannot be tolerated
    - If ineffective, switch to the other untried option or try both in combination
    - If ineffective, refer to a pain specialist and try oral tramadol/topical lidocaine (DO NOT START ANY OTHER OPIOIDS)
    - Carry out regular clinical reviews with a view to reducing treatment doses if sustained pain reduction and also to assess QOL status:
      - Adverse effects
      - Daily activities and participation e.g. work, driving
      - Mood
      - Quality of sleep
      - Patient’s views on their overall condition and any improvements
      - For diabetic neuropathy: duloxetine/amitryptiline, pregabalin, refer if persistent

Other Treatments for Pain

- Ketamine: usually used as a paediatric anaesthetic but has good analgesic properties at subtherapeutic doses. Specialist use for severe pain disorders and palliative care. High incidence of psychosis, abuse and dependence. Can cause CV problems, glaucoma, and laryngospasm.

- Capsaicin cream: excellent topical analgesic but can cause an unpleasant burning sensation.

- Nerve blocks/local anaesthetic wound infusions/epidural anaesthesia

- Physiotherapy, TENS, acupuncture, massage, hot and cold compresses, rest/mobilisation

Post-Operative Analgesia

- If given GA only
  - Mild to moderate pain: paracetamol + NSAIDS/COX-2 +/- weak opioids
  - Severe pain: paracetamol + NSAID/COX-2 + strong IV opioid via PCA/regular syringe driver

- If nerve block/spinal/epidural used too
  - NSAID/COX-2 + strong IV opioid + continue nerve block via PCRA/PCEA

- As patients begin to recover step them down the analgesic ladder gradually, with a view to oral switch ASAP e.g. IV morphine \(\rightarrow\) Oromorph \(\rightarrow\) codeine/tramadol \(\rightarrow\) cocomal/paracetamol alone

- Explain that they must keep taking medication as prescribed even if they have no pain at the time

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