MANAGEMENT OF CANCER PAIN

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CURRENT EVIDENCE BASED CONCEPTS:
- Pain is a frequent complication of cancer, and is common in many other life-limiting illnesses.

PAIN – AN UNMET CLINICAL NEED IN CANCER: THE EPIC SURVEY
- Cancer pain is often poorly recognised and treated
- Phase 1: EPIC survey evaluated pain in 4947 people with cancer
  - Prevalence of pain was 72.7%
  - 23.1% received no pain medication
- Phase 2: EPIC in depth analysis in 573 people
  - Incidence of breakthrough pain 63.7%
  - 58.7% experience pain frequently

CURRENT EVIDENCE BASED CONCEPTS:
- Pain that is not well controlled
  - significant distress and disability
  - despite the availability of best practice approaches to pain management
  - wide variability in how pain is treated in practice

CURRENT EVIDENCE BASED CONCEPTS:
- Increasing complexity of cancer treatment (longer survival of patients)
- Pain before diagnosis
- During treatment
- Chronic pain after cancer treatment
- Advanced cancer/terminal care

PAIN IS THE MOST COMMON TREATABLE SYMPTOM OF CANCER

CURRENT EVIDENCE BASED CONCEPTS:
- Cancer pain approach
  - Holistic
  - Multimodal
  - Mechanism-based
  - Starts at diagnosis

PRINCIPLES OF PAIN MANAGEMENT — WHO 3 STEP LADDER

WHAT IS THE APPROACH TO HIS PAIN?
- Take a good history
- Examination
- Appropriate investigations
- What is the cause of his pain
- High index of suspicion that it is cancer
- What are appropriate treatment options
  - Immediate
  - Longterm
- Minimising treatment side effects
- Education on Pain and its management
- Looking at the ‘whole person’

A TWO STEP ANALGESIC APPROACH
- Patients receiving Step 3 opioids early had superior pain relief
- Fewer patients receiving Step 3 opioids early were dissatisfied with therapy

SUMMARY
- The prevalence of chronic pain is high
  - Up to 80% of patients report chronic pain following surgery
- Many patients do not receive adequate pain control
- Chronic pain is best managed using a multimodal approach
- The WHO analgesic ladder if implemented can be effective in 80%–90% of patients
- Early escalation to Step 3 of the WHO ladder may provide benefits to patients’ analgesia and quality of life

MOST CANCER PATIENTS AROUND THE WORLD STILL DO NOT HAVE ADEQUATE PAIN RELIEF
WHY?
Barriers to Effective Pain Management

- Clinician Related
  - Uncertainty about the role of opioid therapy
  - Misconceptions about opioids
  - Lack of formal pain assessment procedures
- Patient Related
  - Ineffectual pain reporting
  - Fear of opioid drugs
  - Poor compliance
- Systems Related
  - Lack of opioids/adjuvant drugs
  - Lack of MDT approach
  - Lack of pain Mx as a priority

Effective Pain Management

- Good pain assessment by clinicians
- Adequate understanding of opioid pharmacology
- Understanding the myths surrounding opioid use
- Understanding the use of adjuvant medications
- Pro-active in talking to patients about known barriers at the time of introducing pain management
- Treating drug side-effects effectively
- Process of follow up and ongoing management

Mechanistic Approach to Cancer Pain Management:

The four step approach, Lickiss 2001

Based on adequate assessment and diagnosis of the mechanism of pain

1. To identify and reduce the noxious stimulus
2. Psychosocial assessment of the patient
3. Optimise opioids
4. Co-analgesics, including neuropathic pain

Case 1: How would you manage his pain?

- Opioid titration with Morphine (equiv)
  - Constipation: route of opioids and bowel care
- Regular laxatives
- Paracetamol
- NSAID with gastro protective agent (PPI)
- Bisphosphonates: monthly for 3-6 months
- Radiotherapy if isolated area or
- Psychosocial status?
- Education (analgesics/ opioid fears / side effects)

Pharmacology of Cancer Pain

- Never opioids alone!
- Opioids
- Paracetamol
- NSAID’s
- Steroids
- Adjuvants
  - TCA / Anticonvulsants / NMDA antag / anti-tumour therapies
- Novel therapies
- Anti-cancer therapies (chemo, RT, hormonal, targeted)
UNFOUNDED FEARS OF MORPHINE

- Abuse of morphine linked with its therapeutic use
- Addiction (physical dependence / psychological addiction)
  - Too early in the course of the disease
    - Morphine can be continued for many months
    - When pain subsides morphine can be weaned down and discontinued
    - Continues to be effective in the terminal stage
- Excessive sedation
- Respiratory depression

UNFOUNDED FEARS OF MORPHINE

OPIOID PRECISION

- Respiratory depression
- Confusion
- Mental clouding
- Drowsiness
- Inattention

OPIOID PRECISION

MECHANISM FOR EFFECT ON DYSPNOEA:

- Not reduction of ventilatory rate, overall ventilation or sedation
- Can depress respiration but an effect of rate of rise of the opioid dose (titration rate)
- Steady state level of opioid
  - Negligible effect on respiratory drive
  - And on sedative effects
  - Hallenbeck, JPM, 2012
- Pain: stimulant to respiratory drive

OPIOIDS ON RESPIRATION

BREAKTHROUGH PAIN

- Important to allow for breakthrough pain
- Limited by type, duration and half life of opioids
- Adjuvants and cancer treatments important

CASE 1: HOW WOULD YOU MANAGE HIS PAIN?

- Opioid titration with Morphine (equiv)
  - Constipation: route of opioids and bowel care
    - Regular laxatives
    - Paracetamol
    - NSAID with gastro protective agent (PPI)
    - Bisphosphonates: monthly for 3-6 months
    - Radiotherapy if isolated area or
    - Does he have neuropathic pain?
    - TCA or anticonvulsants
    - Steroids: 4 mg or 8-16mg if cord compression
    - Surgical decompression if cord compression followed by RT (timing)
    - Chemotherapy may be considered if widespread disease
    - Education (analgesics/ opioid fears / side effects)
    - Psychosocial status?

PREVALENCE OF OPIOID SIDE EFFECTS IN 150 PATIENTS WITH SEVERE CANCER PAIN

Pool et al, ASCO 2001
IS ORAL MORPHINE STILL THE FIRST CHOICE OF OPIOID FOR MODERATE TO SEVERE CANCER PAIN: A SYSTEMATIC REVIEW WITH THE EPCRC GUIDELINES PROJECT 2010

- No further information to previous Cochrane review: limitation of efficacy and tolerability data
- Oral morphine, oxycodone and hydromorphone have similar efficacy and toxicity in this patient population

ADJUVANTS

- Paracetamol
  - Mixed evidence base for its efficacy in cancer pain
  - Should be used with opioids especially in the titration phase
- NSAID’s
- Antidepressants
  - NNT 2.5 (non cancer studies)
- Anticonvulsants
  - NNT 3 (non cancer studies)
  - Gabapentin / Lyrica
- NMDA receptor antagonists
- Steroids
- Antispasmodic drugs

AUSTRALIAN PAIN SOCIETY EVIDENCE-BASED RECOMMENDATIONS FOR THE PHARMACOLOGIC MANAGEMENT OF NEUROPATHIC PAIN:

- Noradrenergic antidepressants: Nortryptiline, desipramine, amitryptiline, venlafaxine, duloxetine
- Calcium channel alpha 2-delta ligands Gabapentin, pregabalin
- Sodium channel antagonists Topical (and intravenous) lignocaine
- Opioid agonist Morphine, oxycodone, methadone
- Partial opioid agonist Tramadol

ANTI-CANCER TREATMENTS

- Bisphosphonates
  - NNT 11 at 4 weeks, 7 at 12 weeks
- Radiotherapy
- Chemotherapy
- Hormonal
- Targeted therapies
- Radiopharmaceticals

PAIN INTERVENTIONS

- TENS
- Massage, acupuncture
- Regional blocks and neurolytic blocks
  - Celiac plexus, intercostal, trigger points
- Spinal analgesia (opioids and anaesthetics)
  - Epidural catheter, Intra-thecal
- Surgical procedures
  - Decompression
  - Vertebro-plasty

PSYCHOLOGICAL ASSESSMENT AND SUPPORT

- The relationship of pain experience and the whole person
- The psychological status of a person impacts on their pain perception and pain behaviour
- Effect on the emotional and psychological well being
- Effect on relationships, social responses
- Impact on work, financial security, recreation
**Assessment of their psychological and psychosocial dimensions**
- Assess level of anxiety or depression
- Prior coping mechanisms
- Enquire about support structure
- The impact of: breaking bad news, progression of disease
- Treat pathological anxiety and/or depression
- Ongoing support (psychosocial, spiritual)
- Education: pain, meaning, significance of pain, side effects, myths

**Cancer Pain Summary**
- The majority of cancer pain can be effectively treated with available drugs and best practice management strategies
  - which includes regular assessment of pain
- Comprehensive approach begins at diagnosis
- Mechanism-based
- Multimodal management that is patient centred and individualised

**Cancer Pain Summary: cont’d**
- For moderate to severe cancer pain
  - “around the clock” coverage by long-acting strong opioids
  - availability of “as needed” doses of immediate release opioids continues to be recommended as best practice. (Dy SM 2010)
  - pre-emptive doses of immediate release opioids for predictable episodes of breakthrough pain. (Caraceni 2012)

**Cancer Pain Summary: cont’d**
- Recent evidence-based guidelines for neuropathic pain
  - first line adjuvant treatment
    - antidepressants, either tricyclics, or duloxetine or venlafaxine,
    - anticonvulsants, either gabapentin or pregabalin
    - amitriptyline and gabapentin are the two agents recommended for neuropathic pain in recent guidelines from the European Association of Palliative Care
  - Opioids are also effective in neuropathic pain, and may be co-administered as first line treatments, alongside adjuvants
- (Care search)