Advances in Acute Pain Management

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What's Coming Up?

- 'Advances' in Acute Pain Management
  - Novel ways of administering old medicines
  - Some new therapies and evidence
- What do we already know about acute pain management?
  - Multimodal analgesia
- Brief overview of PONV prophylaxis

Why Manage Acute Pain?

- To prevent negative psychological and physiological consequences
  - Pain and suffering (incl. persistent pain)
  - Pneumonia
  - Impaired GI motility
  - Impaired wound healing
  - Tachycardia/Hypertension
  - Prevent ongoing pain

Incidence of Persistent Pain following Surgical Procedures

Type of Operation	Incidence (%)
Amputation	30 to 85
Thoracotomy	5 to 67
Mastectomy	11 to 57
Cholecystectomy	3 to 56
Inguinal Hernia	0 to 63
Vasectomy	0 to 37
Dental Surgery	5 to 13

Advances in Acute Pain Management

- Slow progress despite considerable Pharma investment
  - Potential they may withdraw completely?
- Most new analgesic therapies look to reduce the adverse effects of current therapies [1]

Recent Analgesic Developments

- Paracetamol IV
  - (Propacetamol)
  - Perfalgan
- Diclofenac IV (Dyloject)*
- COXIBs
  - Celecoxib
  - Etoricoxib
  - Lumaricoxib
  - Parecoxib (IV)
  - Rofecoxib
  - Valdecoxib
- Targinact
  - Oxycodone plus Naloxone MR
- Tapentadol
  - New opioid analgesic ?effect on NeuP
- Ionsys
  - Fentanyl iontophoretic transdermal system
- Depodur
  - Epidural MR morphine

Paracetamol IV

- Reduce dose in low weight patients
- Manufacturers state: <50kg, use 15mg/kg[2]
- Analgesia not now thought to be blocked by ondansetron[3]

- We use doses based on weight ranges:

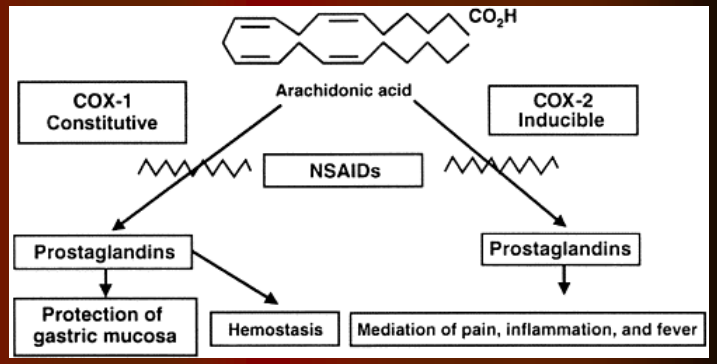
Wt (kg)	<30	30-44	45-50
Dose (mg)	500 tds	500 qds	1000 tds

Dyloject (Diclofenac IV[4])

- Advantages
  - Voltarol requires dilution and buffering before IV admin.
  - Onset of action better than with Voltarol (bolus vs 30 min inf.)
  - Non-inferiority demonstrated
- Disadvantages
  - More expensive than Voltarol*
  - Confusion if multiple diclofenac preps kept
  - Withdrawn in May 2010 following the presence of white particulate matter[4a]

Coxibs

- Initially, widely adopted nationally
- Withdrawal of rofecoxib and valdecoxib signalled massive U-turn
- Along with risks, benefits not as pronounced as hoped
- Etoricoxib and lumaricoxib rarely prescribed
- Note, Pfizer's patent expires in Nov 2014



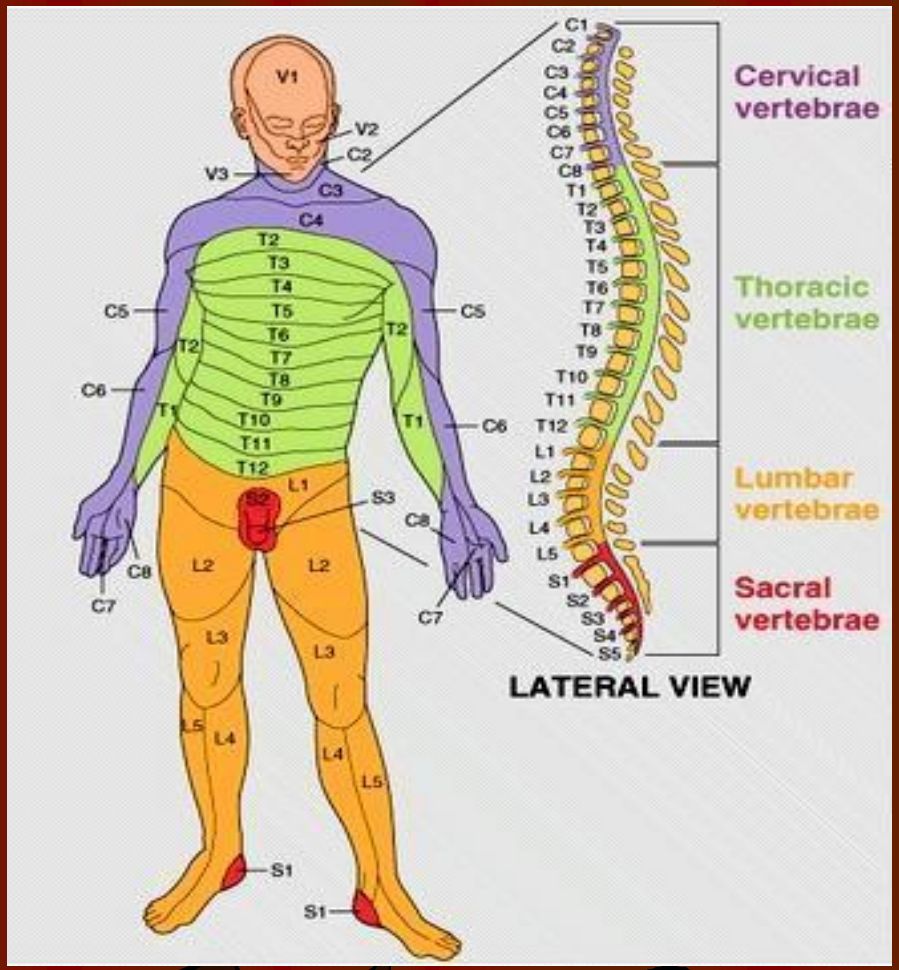
Updates to the Evidence Base

- Regular Opioids in Post-Operative Pain
  - Evidence base poor but audit data may support use
- Spinal Opioids
- Ketamine
- Clonidine
- Dexamethasone[4]
- Adjuvants for NeuP
  - Gabapentinoids

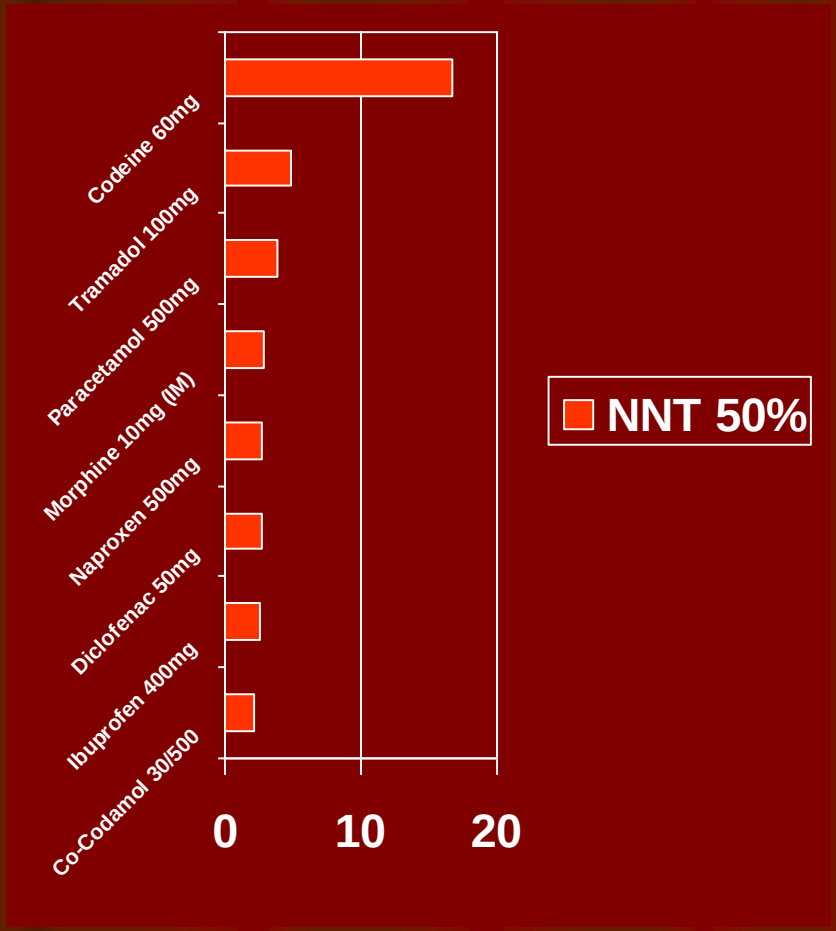
Dexamethasone

- Widely prescribed for PONV
- Recent meta-analysis[4]:
  - Examined high (=>0.21mg/kg), medium (0.11 to 0.2mg/kg) or low (<=0.1mg/kg) doses
  - Reduced post-operative pain in the treatment groups
    - Low dose failed to achieve a statistically significant effect on pain at early (0-4h) pain at rest (-0.33 [-0.70 to 0.04])
  - High and medium doses reduced opioid consumption
  - Pre-operative administration appears to produce a more consistent analgesic effect

Epidural Analgesia (incl. PCEA)



Bandolier League Table of Analgesics



- Notes:
  - In single doses, codeine is not an effective analgesic
  - Tramadol 50mg less effective (NNT=8.3)
  - NSAIDs all have similar efficacy (use the safest!)
  - Don't use IM morphine*

Other Potential Options and Future Therapies

- Ketamine (in sub-anaesthetic doses)
- Acupuncture
- Local anaesthetic infusion devices
  - e.g. ON-Q soaker
- Capsaicin
  - Injectable preparation being trialled in post-operative pain
- Patient-controlled regional anaesthesia

So Where Does This Leave Us?

Multimodal Analgesia[5,6]

Morphine

NSAIDs[7],

Paracetamol[7]

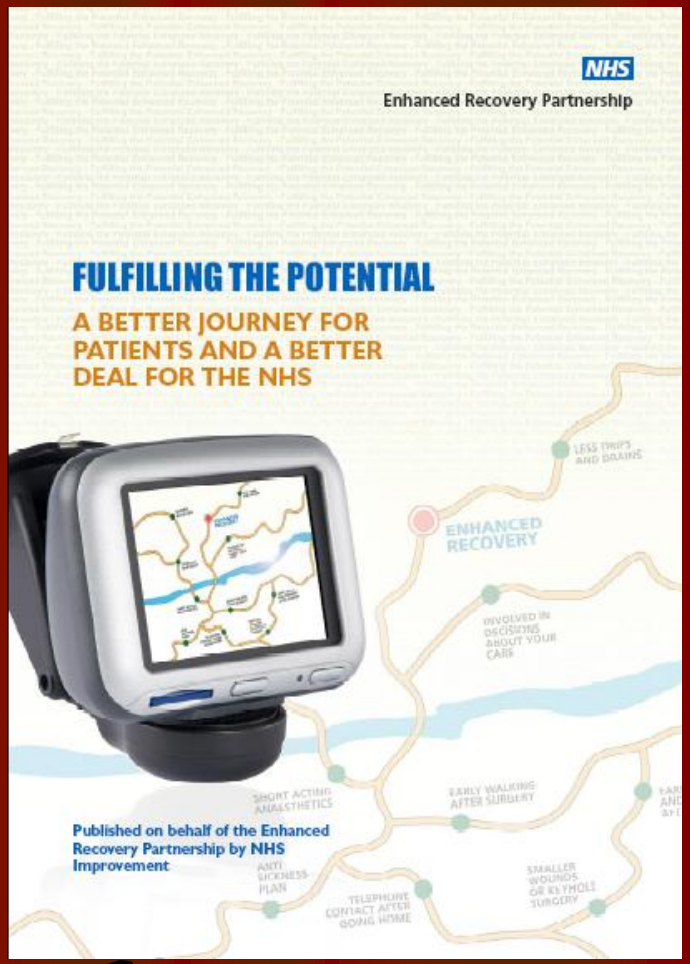
Nerve Blocks

Reduced doses of each analgesic

Improved effectiveness due to synergistic/additive effects

May reduce severity of side effects of each drug

Enhanced Recovery



Enhanced Recovery: Anaesthetic Protocol

- Standardised protocol[8]
- Spinal block
  - Epidural/Spinal
- Rationale
  - Blocks autonomic afferent pathways
  - Pain control
  - Reduce dose of inhalational/IV anaesthetics

Enhanced Recovery: Post-Operative Analgesia

- Keep opioids to a minimum
- Avoid PCA
- Epidural < 48 hours
- IV paracetamol/oral NSAIDs
  - NSAIDs - with or after food?

Tried and Tested Therapies

- Prescribe Regularly:
  - Paracetamol
  - NSAIDs (ibuprofen or naproxen - where not contraindicated) in short courses eg. 3/7
- With Strong Opioid prescribed PRN:
  - eg. oral/sc morphine*
- Place for Other Modalities:
  - Nerve Blocks and Epidurals (& PCEA)
  - PCA or Regular Strong Opioids*

*Aim to limit dose esp. in ERAS; Opioid dose may need reducing in elderly, frail and renal pts & increasing for those on regular strong opioids (including IVDUs)

Resources

- Acute Pain Management: Scientific Evidence[9]
- Clinical Pharmacy and Therapeutics
  - Chapter on Pain by R. Knaggs and G. Hobbs
  - Edited by R. Walker and C. Edwards

Family mis-Fortunes

We asked 100 patients what their main concern about post-operative recovery was.

Our survey said….

1.

2.

3.

4.

5.

What do patient's want?
Concerns during post-op recovery[10]

Importance of factor		Principal factor
Emesis	40%	72%
Pain/aches	29%	9%
Dysphoria	16%	4%
Extra cost	10%	2%
Mental acuity	5%	4%

Apfel Risk Scoring System[11]

- Patient Scores One Point for Each Risk Factor
  - Female Gender
  - Non-Smoking Status
  - Post-Operative Opioid Use
  - Previous History of PONV or Motion Sickness
- Good Correlation between Incidence of PONV and Number of Risk Factors

Correlation between risk factors and PONV

Risk Score	0	1	2	3	4
PONV Risk	10%	20%	40%	60%	80%
Level	Low	Low	Med	High	High

Apfel suggested that any patient scoring 2 or more should receive prophylaxis

Consensus Guidelines (Gan *et al*, 2003[12])

Risk Score	0	1	2	3	4
PONV Risk	10%	20%	40%	60%	80%
Antiemetics	0	0	1/2/3	2/3	2/3

Evidence Base – Impact[13]

- Large Patient Numbers (n=5199)
- All High Risk Patients
  - risk score=2 or more
- Most (n=4123) were randomised to received combination of 6 prophylactic interventions
  - 64 different treatment combinations (2^6)
  - Remainder received comb.'s of first 4 interventions

Evidence Base – Impact[13]

- Ondansetron 4mg
- Dexamethasone 4mg
- Droperidol 1.25mg
- Propofol
- Nitrogen
- Remifentanyl

- No Ondansetron
- No Dexamethasone
- No Droperidol
- Inhaled Anaesthetic
- Nitrous Oxide
- Fentanyl

Evidence Base – Impact[13]

Antiemetics (number)	0	1	2	3
Incidence of PONV	52	37	28	22

Evidence Base – Impact Trial[13]

- Each agent reduced incidence of PONV by around a quarter (26%)
- No agent was found to be more effective than any other
- Combination of avoiding nitrous oxide and propofol use (TIVA) reduced risk by 26%
- No advantage with remifentanyl

PONV: Summary

- Prophylaxis indicated for high risk patients using a combination of anti-emetics
  - I would suggest all should receive one agent
- There is little to choose between antiemetics used*
- Anti-emetics used for treatment should target a different site of action to those used for prophylaxis
- Sufficient evidence is now available to guide management of PONV
- Prophylaxis is key - Treatment is often difficult: use policies

Take Home Messages

- Multimodal analgesia is still important
- Opioids widely used but low opioid techniques may reduce adverse effects and length of stay
- Modified-release opioids may have a place
- Ketamine may be a useful adjunct in resistant pain cases

Take Home Messages (for discussion)

- Developments in acute pain management are few and far between in recent years
- Acute pain management is often less complex than it is time-consuming*
- Good quality pain assessment is key
  - Along with pain scoring and action when scores are high

Take Home Messages (for discussion)

- Chronic pain patients continue to present some of the biggest challenges
- This includes opioid users
  - If on regular opioids, may need increased PRN doses
  - Recreational users often most difficult to manage
    - Continue regular opioid (nb. Subutex)
    - Baseline analgesia (adding tramadol may help)

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