Pain, Older People, Opioids and OTC Drugs

Dr Tim Semple

Grey Matters
clinical scenario

Request - to provide inpatient pain review for female, 92yrs with severe nonsurgical abdo pain, unresponsive to oxycodone, agitated+++  

Background – nursing home resident with moderate dementia, widespread musculoskeletal pains on fentanyl patch 150mcg/hr (!)  

Further background - had been on Panadeine Forte 6/day for 2 yrs, changed to fentanyl patch 25mcg/hr 6 months earlier  

Initial benefit but dose escalation after 2 months, then monthly
Outcome....

No major pathology found

Presumed opioid-induced agitation/pain
Settled with rapid reduction/cessation of fentanyl dose
Conversion to buprenorphine patch 10mg weekly

Nursing home prescriber surprised when informed of daily oral morphine equivalence of 500mg causing severe pain state
So how did we get here?
Unrealistic prescriber and patient expectations of benefit from opioids
Current thinking on efficacy and role of opioids for chronic pain

4 systematic reviews and meta-analyses 2004-2008

NNT > 2.5 .......only 2 out of 5 patients with CNCP benefit

– not “painkillers”
– usual analgesic benefit 20 - 30%, if component of multimodal approach
– encourage weaning after 3 – 6 months
What has changed with the pain medicine viewpoint of opioids for CNCP?

- Evidence for benefit less than expected

- Evidence for harm greater than expected
The “big picture” behind the clinical scenario

• Prevalence of pain in elderly - undertreated

• Rapid escalation of opioid use in elderly over past decade

• Adverse events associated with opioids

• Impact of prior longterm codeine intake initiating tolerance

• Shortfalls in knowledge of and access to non-pharmacological pain management options
Latest health survey results for chronic conditions
### South Australia

**ABS Catalogue 4364.0.55.001**

<table>
<thead>
<tr>
<th>Selected Health Characteristics (Estimate)</th>
<th>2007-08</th>
<th>2011-12</th>
</tr>
</thead>
<tbody>
<tr>
<td>High/Very high psychological distress <em>(b)(c)</em></td>
<td>154,600</td>
<td>142,900</td>
</tr>
<tr>
<td><strong>Selected current long-term conditions (d)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis <em>(e)</em></td>
<td>272,400</td>
<td>271,900</td>
</tr>
<tr>
<td>Asthma</td>
<td>154,400</td>
<td>174,200</td>
</tr>
<tr>
<td>Back pain/problem, disc disorder <em>(f)</em></td>
<td>232,900</td>
<td>240,900</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease <em>(g)</em></td>
<td>37,200</td>
<td>38,100</td>
</tr>
<tr>
<td>Deafness <em>(h)</em></td>
<td>180,100</td>
<td>178,600</td>
</tr>
<tr>
<td>Diabetes mellitus <em>(i)</em></td>
<td>73,200</td>
<td>76,200</td>
</tr>
<tr>
<td>Hayfever and allergic rhinitis</td>
<td>269,900</td>
<td>318,700</td>
</tr>
<tr>
<td>Heart, stroke and vascular disease <em>(j)</em></td>
<td>93,700</td>
<td>83,300</td>
</tr>
<tr>
<td>Hypertensive disease</td>
<td>176,500</td>
<td>183,000</td>
</tr>
<tr>
<td>Kidney disease <em>(k)</em></td>
<td><strong>1000</strong></td>
<td>11,700</td>
</tr>
<tr>
<td>Long sightedness</td>
<td>434,000</td>
<td>507,600</td>
</tr>
<tr>
<td>Malignant neoplasm (cancer)</td>
<td>26,000</td>
<td>20,300</td>
</tr>
<tr>
<td>Mental and behavioural problems <em>(l)</em></td>
<td>190,800</td>
<td>238,800</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>49,300</td>
<td>63,800</td>
</tr>
<tr>
<td>Short sightedness</td>
<td>305,500</td>
<td>352,100</td>
</tr>
</tbody>
</table>

*“I have back pain”* - 240,900
*“I have arthritis”* – 271,900
Survey of 6700 elderly Swedes

None or mild chronic pain – 77%

Moderate chronic pain – 19%

Severe chronic pain – 4%
EQ-5D index measures 5 dimensions of health-related quality of life (HRQoL)

- HRQoL severely impacted by chronic pain
Prevalence, Causes, Severity, Impact, and Management of Chronic Pain in Australian General Practice Patients

Henderson et al, BEACH program 2013

192 GPs, 5800 patients

20% of patients report chronic pain

osteoarthritis - 50%

back pain - 30%
66% of GP pain workload in patients > 65yrs
“Medication only “ in 56% reflects unrealistic expectations of benefit of medication
Underutilisation of paracetomol

Panadeine Forte 1st place (2.2 % of adult NSW population)

High popularity of oxycodone (1.2% of adult NSW population!)
Apparent under-utilisation of nonpharmacological options

Referral only “3.7%”

Difficult to distinguish between “quality prescribing” or not
11,000 DVA clients dispensed oxycodone in 2010

Initiation of a strong opioid (oxycodone) occurred in over 1/3 community-living DVA clients without prior simple analgesics or weak opioids
morphine Vs oxycodone 2002 – 2008
• oxycodone becomes preferred strong opioid – why?
• greatest increases in 80+ age group

Roxburgh et al MJA Sept 2011
Labelled as “PHARMAGEDDON” of successful marketing in the USA

Commercial triumph despite $670 million fine for “false marketing” in USA

Amphetamine-like effects in some = increased likeability
Canada bans Oxycontin – May 1, 2012
Highlights increases in fentanyl-related deaths in younger IVDU population
Rapid escalation of fentanyl patch use in 80yrs + population – appropriate or not?

Clinician concerns re rapid tolerance to fentanyl

**Figure 1.** Fentanyl prescriptions per 1000 population in Australia. Includes 12, 25, 50, 75 and 100 μg h⁻¹ transdermal patches. Source: Drug Utilisation Sub-Committee of the Pharmaceutical Benefits Advisory Committee.
Association between mental health disorders, problem drug use and regular prescription opioid use

- Common mental health disorders increase likelihood by 3 X of later initiation of prescription opioids for pain

- Problem drug use increases likelihood to a significantly lesser extent of prescription opioids for pain

“Undertreated mental health disorder patients prescribed opioids in response to high levels of distress”
Adverse Selection? A Multi-Dimensional Profile of People Dispensed Opioid Analgesics for Persistent Non-Cancer Pain

Kris D. Rogers¹,²*, Anna Kemp³, Andrew J. McLachlan⁴,⁵, Fiona Blyth¹,²,⁵

¹ The Sax Institute, Sydney, New South Wales, Australia, ² Sydney Medical School, University of Sydney, Sydney, New South Wales, Australia, ³ School of Population Health, The University of Western Australia, Perth, Western Australia, Australia, ⁴ Faculty of Pharmacy, University of Sydney, Sydney, New South Wales, Australia, ⁵ Centre for Education and Research on Ageing, Concord Hospital, Sydney, New South Wales, Australia

PBS Prescription review 2006 – 2009 of 100,000 patients “45 and Up” cohort

50% over 70yrs

5% on longterm opioids

5% on intermittent opioids

PLOS ONE Dec 2013
Adverse selection in opioid dispensing

Opioid dispensing associated with

– younger age group (45-49yrs)

– treatment of osteoarthritis

– smoking / obesity / lower levels of physical activity

– lower income / reduced private health insurance rates

– living outside major city

– psychological distress
Prospective cohort study of 1500 patients dispensed opioids

- strong association with psychological distress, poor health and lower income

- social and psychological factors more significant in younger patients

NDARC team - PAIN Feb 2015
• Home Medicines Review data analysed 2010-2012

• 10,444 reviews of > 60yrs

• 2711 taking opioids

• 1816 taking regular dose opioids

Poster presentation ASEAPS 2013
Nearly 10% taking > 120mg oral morphine equivalents daily

Over 50% on additional anxiolytics/hypnotics

Optimised paracetamol in only 50%

<table>
<thead>
<tr>
<th>Patient characteristics based on daily MEQ dose</th>
<th>≤120mg PO MEQ</th>
<th>&gt;120mg PO MEQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>1659 (91.4%)</td>
<td>157 (8.6%)</td>
</tr>
<tr>
<td>Mean age*</td>
<td>76.3 (±8.6)</td>
<td>74.0 (±8.7)</td>
</tr>
<tr>
<td>MEQ PO dose (mg)**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (±SD)</td>
<td>33.5 (±25.4)</td>
<td>238.9 (±121.5)</td>
</tr>
<tr>
<td>Median</td>
<td>27mg</td>
<td>180mg</td>
</tr>
<tr>
<td>Anxiolytic and/or hypnotic**</td>
<td>39.3%</td>
<td>56.1%</td>
</tr>
<tr>
<td>Antidepressants and/or antipsychotics**</td>
<td>44.2%</td>
<td>64.3%</td>
</tr>
</tbody>
</table>
Medicine Review of nursing home residents

7177 assessed

11% taking > 120mg MEQ/day
90% with analgesic therapy – 28% on opioids

Mean MEQ/day 56.5mg

<table>
<thead>
<tr>
<th>Analgesic therapy</th>
<th>6526 (90.5%)</th>
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<tbody>
<tr>
<td>Analgesic use in patients who have at least 1 pain condition</td>
<td>6513 (90.7%)</td>
</tr>
<tr>
<td>Analgesic use in RACF residents who have at least 1 pain condition</td>
<td>6513 (90.7%)</td>
</tr>
<tr>
<td>NSAID</td>
<td>426 (5.9%)</td>
</tr>
<tr>
<td>Adjunct agents</td>
<td></td>
</tr>
<tr>
<td>Tricyclic antidepressant (TCAs)</td>
<td>391 (5.4%)</td>
</tr>
<tr>
<td>Pregabalin/gabapentin</td>
<td>33 (0.5%)</td>
</tr>
<tr>
<td>Serotonin-noradrenalin reuptake inhibitors</td>
<td>439 (6.1%)</td>
</tr>
<tr>
<td>Optimised paracetamol</td>
<td>2867 (39.9%)</td>
</tr>
<tr>
<td>Opioids (RD and/or PRN)</td>
<td>2796 (39.0%)</td>
</tr>
<tr>
<td>RD opioids</td>
<td>28% (56.5mg MEQ/D)</td>
</tr>
<tr>
<td>RD opioids and optimised paracetamol</td>
<td>56%</td>
</tr>
<tr>
<td>RD opioids and anxiolytics/hypnotics</td>
<td>978 (48.3%)</td>
</tr>
</tbody>
</table>
2-fold increase in fracture risk if MEQ/day > 50mg

One in ten of individuals on > 50mg will have a fracture each year
10 chronic LBP patients given oral morphine ( < 100mg) for 4 weeks then ceased

Functional MRI at baseline, one month, four months

Control group – no opioids
Gray matter brain changes after 4 weeks

- Dose-related volume decrease in amygdala
- Dose-related volume increase in hypothalamus, frontal gyrus, pons
- Structural and functional changes in reward- and affect-processing circuitry

Most changes sustained at 4 months
Longstanding belief - slow-release long-acting opioids are preferable to intermittent short-acting opioids for CNCP

Challenged by failure to prove improvements in -

- safety
- efficacy
- QOL
- pain stability
- sleep

M Sullivan Pain 2014
Combination NSAID-codeine preparations and gastrointestinal toxicity

Claire Evans, Teresa A Chalmers-Watson, Richard B Gearry
Codeine-induced hyperalgesia and allodynia: investigating the role of glial activation

JL Johnson¹, PE Rolan¹,²,³, ME Johnson⁴, L Bobrovskaya⁴, DB Williams⁴, K Johnson⁵, J Tuke⁶ and MR Hutchinson⁷

codeine mg : mg activates glia as much as morphine

glial activation initiatives tolerance and hyperalgesia

Regular use of codeine for milder pain conditions may lead to as much tolerance and increased pain sensitivity as larger doses of strong opioids
So, what to think about codeine?

- Unpredictable pro-drug with no effect in 5-10% and high effect in 5-10%
- Little evidence of benefit – would not get to market now
- Associated with initiating dependency, especially in combination with NSAID as OTC analgesic
- May induce tolerance rapidly and prevent stronger opioids working when needed
Research papers

Different profiles of buprenorphine-induced analgesia and antihyperalgesia in a human pain model

Wolfgang Koppert\textsuperscript{a,*}, Harald Ihmsen\textsuperscript{a}, Nicole Körber\textsuperscript{a}, Andreas Wehrfritz\textsuperscript{a}, Reinhard Sitt\textsuperscript{a}, Martin Schmelz\textsuperscript{b}, Jürgen Schüttler\textsuperscript{a}

\textsuperscript{a}Department of Anaesthesiology, University Hospital Erlangen, Krankenhausstrasse 12, D-91054 Erlangen, Germany
\textsuperscript{b}Department of Anaesthesiology Mannheim, University of Heidelberg, Theodor-Kutzer Ufer 1-3, D-61087 Mannheim, Germany

Received 7 February 2005; received in revised form 17 May 2005; accepted 20 June 2005

Buprenorphine – quite different from other opioids

potential lower association with tolerance and hyperalgesia

may be a preferable choice if tolerated......

PAIN 2005
Options for managing pain

*APS Pain in RACF – Management Strategies*
Self-management intervention for chronic pain in older adults: A randomised controlled trial

Michael K. Nicholas\textsuperscript{a,*}, Ali Asghari\textsuperscript{a,b}, Fiona M. Blyth\textsuperscript{a,c,d}, Bradley M. Wood\textsuperscript{a}, Robin Murray\textsuperscript{a}, Rebecca McCabe\textsuperscript{a}, Alan Brnabic\textsuperscript{e}, Lee Beeston\textsuperscript{a}, Mandy Corbett\textsuperscript{a}, Catherine Sherrington\textsuperscript{f}, Sarah Overton\textsuperscript{a}

Eight 2 hour sessions – significant improvements in pain disability and distress
The *Pain Course*: A randomised controlled trial of a clinician-guided Internet-delivered cognitive behaviour therapy program for managing chronic pain and emotional well-being

Blake F. Dear \(^a\)*, Nick Titov \(^a\), Kathryn Nicholson Perry \(^b\), Luke Johnston \(^a\), Bethany M. Wootton \(^a\), Matthew D. Terides \(^a\), Ron M. Rapee \(^a\), Jennifer L. Hudson \(^a\)

\(^a\)The Centre for Emotional Health, Department of Psychology, Macquarie University, Sydney, Australia

\(^b\)School of Social Sciences and Psychology, Centre for Health Research, University of Western Sydney, Australia

**Cost-effective, accessible and no side-effects**
In an ideal world ....

- GP confident with pain management skill-base and time available
- Repeated doses of medical consistency – same positive message reinforced about CNCP and prognosis
- Ready access to self-management tools – practice and RACF nurse coaching and consumer support
- Community chronic pain-orientated allied health for pacing / exercise / coping
- Appropriate safe and sustainable analgesic drug management
New national body to lobby government ....

National Pain Strategy

Pain Management for all Australians
Australian government review

Pharmaceutical drug misuse strategy March 2012