Literature Review: Chronic Opioid Therapy for Non-cancer pain

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Disclosures

- PsychU: consultant
- Otsuka pharmaceutical: consultant (Abilify Maintena, Rexulti)
- Litigation consultant: “Expert witness” for US DOJ & civilian cases
- Buckeye Community Health Plan: pharmacy & therapeutics committee
Objectives

- Opioid nomenclature
- Efficacy for chronic non-cancer pain (CNCP) & side effects
- Review of CDC guidelines
Nomenclature

- Opium: dried powdered mixture of 20 alkaloids from the seed capsules of the poppy
- Opiate: any agent derived from opium (really only 3: codeine, morphine, thebaine)
- Opioid: all substances with morphine like properties
Whatever they’re called, at least they work…

- In a large epidemiologic study in Denmark, chronic pain patients using opioids had worse pain, higher health care utilization and lower activity levels than matched chronic pain patients not using opioids.¹

- Opioid use may go against important principles of chronic pain management including increased self-efficacy, reduced reliance on the health care system, reinforcement of pain behavior, and passivity and loss of autonomy by externalization of the locus of control.²


…or maybe not.

- A systematic review of randomized trials for multiple opioids utilized for managing various chronic pain conditions, showed fair evidence for tramadol in managing osteoarthritis. For all other conditions and all other drugs excluding tramadol, the evidence was poor based on either weak positive evidence or indeterminate or negative evidence.

What does the evidence say?

- A 3-year registry study of opioids for CNCP found that only 5% of 233 patients who were on >100mg of oxycodone/day were able to have sustained analgesic benefit.¹

- A 12-month follow-up study on patients with CNCP, previously opioid-naïve, treated with transdermal fentanyl or transdermal buprenorphine found that only 11-13% had sustained pain relief at 6 months.²

What does the evidence say?

- “There have been inconclusive results on the efficacy of long-term opioid therapy in patients with chronic pain but moderate level evidence of dose-dependent risk of harm.”

- For patients with diabetes, higher total opioid dose was strongly associated with poorer outcomes including HgbA1C level, LDL, any hospitalization, any diabetes-related hospitalization and any ED visit.


Myths & Facts (www.responsibleopioidprescribing.org)

<table>
<thead>
<tr>
<th>Myth: Chronic opioid therapy is supported by strong evidence</th>
<th>Fact: Evidence of long-term efficacy is limited and of low quality</th>
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</thead>
<tbody>
<tr>
<td>Physical dependence only occurs with high doses over months</td>
<td>With daily use, dependence can occur in days or weeks</td>
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<tr>
<td>High dose ($\geq$120 mg of morphine/day) therapy is supported by strong evidence</td>
<td>No randomized trials show long-term effectiveness in CNCP</td>
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Fibromyalgia

- 2016 SR:
  - “No evidence from clinical trials that opioids are effective”
  - “patients with FM receiving opioids have poorer outcomes than patients receiving nonopioids, and FM guidelines recommend against the use of opioid analgesics”
  - “Despite this, and despite the availability of alternative FDA approved pharmacotherapies and the efficacy of nonpharmacologic therapies, opioids are commonly used in the treatment of FM.”

Buprenorphine?

- A 2013 Cochrane review evaluated the effectiveness of transdermal buprenorphine for low back pain and found very low quality evidence with no difference vs placebo for improvement in function.¹
- A 2014 study² showed that patients (N=35) with very high opioid requirements (200-1,370 MEQ/day) were able to successfully transitioned to buprenorphine SL.
  - At 2 month follow-up, mean pain score decreased from 7.2 to 3.5, 34/35 patients reported a decrease in pain, and 35/35 reported increased QOL. Mean dose of buprenorphine is 28mg ± 6 mg/day.

“High dose” opioids

- The notion of 100mg or 120mg of MEQ as “high dose” is not based on any discernible evidence. Rather it is likely more related to the psychological concept of “digit preference” where numbers that end in “5” or “00” are preferred.¹

- A 2016, prospective observation cohort study evaluated the impact of high-dose opioid analgesics on overdose mortality. It found there was no “cut off” and that mortality increased gradually across the entire range of MEQs. Further rate of overdose death was 10x higher in those who were co-prescribed benzos.²


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“High dose” opioids

- 8.6% of patients with CLBP receive high-dose opioids (≥100mg/day of ME). The median dose is 180mg/day.¹

  - Only 23% of patients on high dose opioid therapy were seen in a pain clinic.

- In a study of 9,940 adults receiving long-term opioid therapy for CNCP, those who received 100mg/day or more of morphine equivalents had an 8.9x greater risk of overdose.²

CDC Guideline for Prescribing Opioids for Chronic Pain (March 18, 2016)

- 20% of patients presenting to PCP with NCP receive an opioid prescription
- Chronic pain as >3 months
- 3-4% of US adult population is prescribed COT
- Directed to PCPs prescribing COT for adult CNCP as outpatients
  - PCPs provide 50% of all opioid prescriptions
- Address 5 primary clinical questions


1. Effectiveness of long-term therapy

- Short-term effectiveness is established
- Insufficient evidence to determine if there is efficacy over placebo
  - Strong evidence of dose-dependent harm
2. Risk of abuse, addiction, overdose

- In primary care setting, risk of opioid dependence 3-26%
- In pain clinic settings, risk is 2-14%.
  - Risk factors: h/o SUD, younger age, mental illness
- Significantly increased, dose-dependent risk of overdose (vs placebo)

3. Comparative effectiveness of opioid dosing strategies

- No differences in efficacy or 1-year outcomes using ER/LA vs IR formulations
- There is a greater risk of non-fatal overdose if initiating with ER/LA vs IR formulations
- Inconsistency with data regarding methadone
  - It has been found to be safer, equivalent and more likely to cause overdose than morphine
4. Predicting/monitoring opioid misuse

- Inconsistent results regarding effectiveness of the Opioid Risk Tool (ORT) and SOAPP-R
- No good evidence regarding effectiveness of risk mitigation strategies in improving outcomes related to overdose, addiction, abuse or misuse
  - UDS, PDMP, pill counts, more frequent monitoring, abuse-deterrent formulations, prescribing agreements, risk assessment tools

5. Effects of opioid therapy for acute pain on long-term use

- Opioid therapy prescribed for acute pain is associated with greater likelihood of long-term use.
CDC: Recommendations

1. Non-pharmacologic and non-opioid therapy are preferred first line treatments
2. Before starting opioids, establish treatment goals for pain and function
3. Discuss R/B/A
4. Begin with IR formulations
5. Reassess therapy if increasing dose to ≥ 50 MEQ
   - “avoid” or “carefully justify” doses ≥ 90 MEQ

CDC: Recommendations

6. For acute pain, use IR opioids up to 3 days, >7 days is “rarely” needed.
7. Re-evaluate R/B within the first month of starting and every 3 months thereafter
8. Evaluate risk factors for misuse before starting
9. PDMP at start and at least every 3 months
10. UDS at initiation and at least annually
11. Avoid opioids + benzos “whenever possible”
12. Use MAT for opioid use disorder
HOW TO TELL WHEN THERE'S SOMETHING FISHY ABOUT YOUR PHARMACY

WHAT DO YOU HAVE FOR EAR WAX REMOVAL?

OXYCONTIN.

DANDRUFF?

OXYCONTIN.

HEMORRHOIDS?

OXYCONTIN.

IS THERE ANYTHING THAT ISN'T CURED BY OXYCONTIN??

OXYCONTIN.

FOR FOOT ODOR WE SUGGEST XANAX.