

Acute & Chronic Pain Management *(requiring opioid analgesics)* **in Patients Receiving Pharmacotherapy** **for Opioid Addiction**

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Program on Opioid Risk Management

Daniel P. Alford, MD, MPH, FACP, FASAM
Boston University School of Medicine
Boston Medical Center

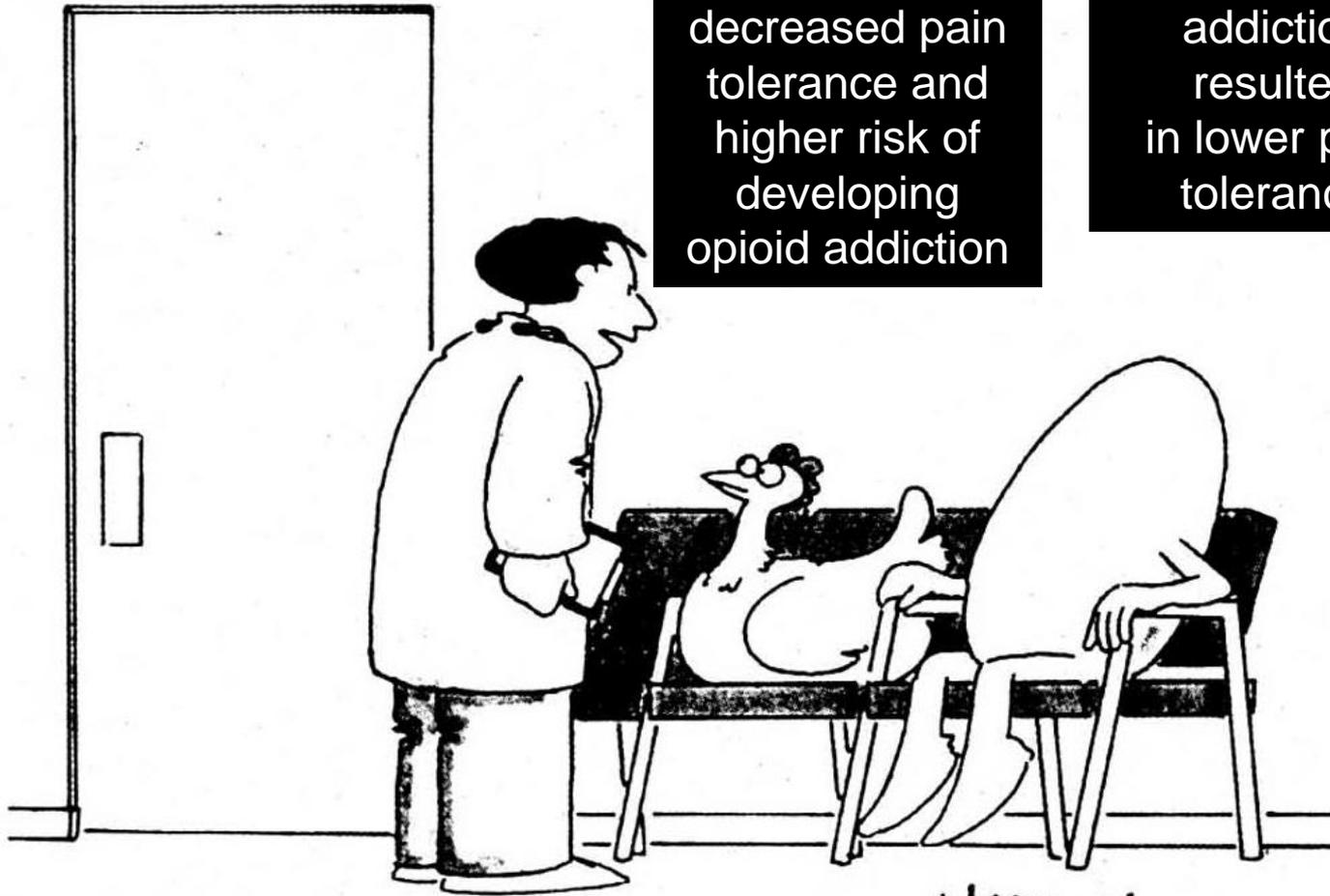


Altered Pain Experience

- Patients with opioid dependence have less pain tolerance than peers in remission or matched controls
- Patients with a history of opioid dependence have less pain tolerance than siblings without an addiction history
- Patients on opioid maintenance treatment (i.e. methadone and buprenorphine) have less pain tolerance than matched controls

Born with
decreased pain
tolerance and
higher risk of
developing
opioid addiction

History of opioid
addiction
resulted
in lower pain
tolerance



HARDIN

“WHO WAS FIRST?”

The “Opioid Debt”

Patients who are physically dependent on opioids (e.g., methadone, buprenorphine) must be maintained on daily equivalence before ANY analgesic effect is realized with opioids used for acute pain management

Acute Pain: Methadone Maintenance Patients

- Methadone maintenance does not confer analgesia
- Opioid analgesics will not cause excessive central nervous system or respiratory depression due to opioid cross-tolerance
- Risk of relapse to active drug abuse may be higher with inadequate pain management than with the use of opioid analgesics

Acute Pain: Methadone Maintenance Patients

- Compared 25 post-surgical MM patients who had received opioid analgesics to 25 MM patient controls matched for age, sex, duration on MM
- After 20 month follow-up, no difference in relapse indicators such as substance abuse patterns and methadone dose changes
- Therefore opioid analgesics may be used safely in MM patients with acute post-surgical pain without compromising addiction treatment

Acute Pain: Methadone Maintenance Patients

- Continue usual methadone dose
- Treat pain aggressively with conventional analgesics, including opioids at higher (1.5 times) doses and shorter intervals
- Avoid using mixed agonist/antagonist opioids (e.g., butorphanol (Stadol)) as they will precipitate acute withdrawal
- Careful use and monitoring of combination products containing acetaminophen

Chronic Pain: Methadone Maintenance Patients

- Advantages
 - Analgesia from methadone dose may be good test for opioid responsive pain
 - Closely monitored in methadone program e.g., drug testing, pill counts
 - Methadone will block euphoric effects of opioid analgesics
- Disadvantages
 - May interfere with drug testing in methadone program e.g., opiates and semisynthetics
 - Opportunities to divert prescribed opioids

Chronic Pain: Methadone Maintenance Patients

- In an idealized world would be able to treat both opioid addiction and chronic pain with methadone dosed TID or QID either in the methadone maintenance program or in primary care

Buprenorphine as an Analgesic

- Sublingual formulation approved for addiction not pain treatment
- Small studies in Europe and Asia demonstrate analgesic efficacy of SL formulation (0.2-0.8 mg q 6-8 h) in opioid naïve post-operative pain
- Analgesic ceiling effect is UNCERTAIN
 - Differing data on analgesic ceiling effect in animal models
 - No published data indicating an analgesic ceiling in humans
 - Doubling dose resulted in dose-dependent increase in analgesia without increase in respiratory depression

Edge WG et al. Anaesthesia. 1979

Moa G et al. Acta Anaesthesiol Scand. 1990

Book SW, Myrick H, Malcolm R, Strain EC. Am J Psychiatry 2007

Theoretical Concern...

- Buprenorphine may
 - antagonize the effects of previously administered opioid analgesics
 - block the effects of subsequent administered opioid analgesics
- Experimental mouse pain model
 - Combination of buprenorphine and full opioid agonist analgesic (morphine, oxycodone, hydromorphone, fentanyl) resulted in additive or synergistic effects

Acute Pain: Buprenorphine Maintenance Patients

The “Five Day” Rule University of Michigan Protocol

- If moderate-severe post-operative pain is anticipated
 - Discontinue buprenorphine and transitioned to short-acting opioid for ≥ 5 days prior to surgery
- But this protocol...
 - Risks causing a disruption in the patient’s recovery from opioid addiction by stopping buprenorphine during preoperative period
 - Has never been evaluated and is based on a theoretical concern of pharmacological principles

Acute Pain: Buprenorphine Maintenance Patients

- 5 patients underwent 7 major surgeries (colectomy, knee replacement, small bowel resection, bilateral mastectomy)
- All maintained on stable doses of SL buprenorphine (2 mg – 24 mg) for chronic musculoskeletal pain – some with remote hx of opioid addiction
- By chart review, postoperative pain was adequately controlled using oral or IV full agonist opioids

Acute Pain:

Buprenorphine Maintenance Patients

Options

1. Continue buprenorphine and titrate short-acting opioid analgesic
2. Discontinue buprenorphine, use opioid analgesic, then re-induce w/ buprenorphine
3. Divide buprenorphine to every 6-8 hours
4. Use supplemental doses of buprenorphine
5. If inpatient, d/c buprenorphine, start methadone 20-40mg, use opioid analgesics, then re-induce w/ buprenorphine

Alford DP, Compton P, Samet JH. Ann Intern Med 2006

Book SW, Myrick H, Malcolm R, Strain EC. Am J Psychiatry 2007

Alford DP. Handbook of Office-Based Buprenorphine Treatment of Opioid Dependence. 2010

Chronic Pain: Buprenorphine Maintenance Patients

- Buprenorphine-maintained patients may not benefit from concurrent opioid analgesics due to high mu receptor affinity
- Due to its inherent analgesic properties, buprenorphine could be dosed every 6-8 hours to treat both opioid dependence (*on-label* indication) and pain (*off-label* indication)

Chronic Pain: Buprenorphine Maintenance Patients

- Open-labeled study of 95 patients with chronic pain who failed long-term opioids and were converted to sublingual buprenorphine
- Mean buprenorphine dose 8mg/d (4-16mg) in divided doses
- Mean duration of treatment ~9 months
- 86% had moderate to substantial pain relief along with improved mood and function
- 6% discontinued therapy due to side effects or worsening pain

Pain:

Naltrexone Maintenance Patients

- Acute Pain
 - Must override mu blockade
 - Complicated issue for long-acting preparations
 - Nerve blocks, epidurals
- Chronic Pain
 - Nonopioids are only option
 - ?low dose (4.5 mg) naltrexone may offer analgesia*

*Younger J, Mackey S "Fibromyalgia symptoms are reduced by low-dose naltrexone: A pilot study" Pain Med 2009.

Next Steps...

- Methadone: how to disseminate best practices for treating acute pain
- Methadone: how to better coordinate care with methadone programs to treat chronic pain and addiction simultaneously
- Buprenorphine: what is optimal strategy for managing acute pain, especially in the perioperative setting
- Naltrexone: what is optimal strategy for managing acute pain, especially in patients maintained on long-acting preparations