Treating Acute Pain in Patients Being Treated for Opioid Use Disorder

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Some Background

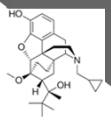
- In 2015, the incidence of opioid use disorder (OUD) in the US was ~1 out of 125 people[1]:
  - Prescription opioids 2,000,000
  - Heroin 590,000
- Opioid OD deaths increased 27% from 2016-2017
- Medication-assisted treatment (MAT) for opioid use disorder is 3 times as effective as sobriety-based treatment alone[2].
- As a result, MAT is spreading rapidly in the US.

[1]Center for Behavioral Health Statistics and Quality (2016). Key substance use and mental health indicators in the US: Results from the 2015 National Survey on Drug Use and Health (HHS Publication No. SMA 16-4984, SDUH Series H-51
[2]Fiellin DA, et al (2014). Primary Care–Based Bup Taper vs Maintenance Therapy for Prescription Opioid Dependence. JAMA Intern Med;174(12):1947-1954.

The Problem

- While MAT helps OUD patients control their addiction, it does so in part by blocking the effects of abused opioids.
- This creates a serious challenge with treating these patients if they develop severe acute pain
- In addition, the use of opioids to treat acute pain can very easily cause relapse, often fatal

MAT Treatments - buprenorphine



- Most widely used MAT Tx; developed for use by PCPs in their offices
- Receptor activity:
  - Mu: partial agonist
  - Kappa: strong antagonist
  - High affinity for both, preventing other opioids from binding
- Pharmacokinetics
  - Eliminated by 1) glucuronation and 2) dealkalination by CYP3A4
  - Both renal and fecal elimination
  - Half-life = 24-48 hours

MAT Treatments: Naltrexone

- Pure antagonist at mu and kappa receptors
- Very high affinity
- Can be used in oral form, but rapid half-life, so it's easy to cheat when on it
  - Primary metabolite, 6β-naltrexol, is also active
  - $T_{½}$: naltrexone = 4 hr 6β-naltrexol = 12 hr
- Primarily used as month-long injection (Vivitrol)
  - Main factor limiting its use: $1200/month!
  - Levels peak 3 hr. after injection, stable 2 wk, then slowly ↓
  - Metabolized in cytoplasm, also glucuronated

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MAT Treatments: Methadone

- Use generally reserved for patients who can't afford or can't comply with other MAT treatments
- Must be prescribed by a federally-designated methadone treatment program
- Usually given high-dose, so tolerance limits response to abuse of other opioids
- Extremely variable response patient-to-patient
- ↑ QTc, potent respiratory inhibitor
- Metabolized by CyP3A4, 2B6, 2C19, 2C9, or 2D6
  - But binds all of them weakly; displaced by other drugs
- *5% of opioid Rx's, 30% of Rx opioid deaths*

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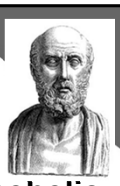
Treating Acute Pain in MAT Patients: General Principles



Remember Hippocrates!
Opioids to MAT patients = vodka to an alcoholic

- Always contact addiction Tx program to confirm dose, collaborate care postop
- Aggressively use all reasonable non-opioid options:
  - Meds, procedures, physical modalities, etc.
- Continue their MAT (except poss. naltrexone IR)
  - Slow loss of opioid blockade could cause a fatal OD
  - Break up methadone or buprenorphine into tid-qid dosing
- If you must use an opioid, use a low-reward one (avoid oxycodone and hydromorphone)
- Avoid outpt. opioid Rx's (lead them not into temptation!)
- If reported pain levels not consistent w/ pathology, consider relapse

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Opioid Alternatives: Acetaminophen

- Can use up to 6g/d for brief periods
  - Better to give scheduled doses, not prn
- Very few ADRs
- Available po, rectal, IV ($$$ - reserve for npo)
- Avoid if serious liver disease or ↑↑ LFTs
  - If mild, use lower doses and monitor LFTs

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Opioid Alternatives: Nonsteroidals

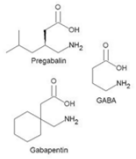
- IV, oral, topical available
- Celecoxib does not inhibit platelets; preferable in conditions where bleeding may occur (surgery, trauma, etc.)
- Indications for gastroprotection:
  - age > 50, Hx PUD/gastritis, DM, neuropathy
- Avoid if:
  - ASA allergy, Hx bleeding ulcer, CKD, coagulation problems

Opioid Alternatives: Muscle Relaxants

- Optimal:
  - Baclofen 10-20 tid
  - Tizanidine (Zanaflex) 2-4 mg tid
  - Metaxolone (Skelaxin) 800 tid-qid
- +/-: (work mostly by sedation)
  - Orphenadrine (Norflex) 100 bid
  - Methocarbamol (Robaxin) 750 2 qid
  - Chlorzoxazone (Parafon Forte) 250-500 tid-qid
  - Cyclobenzaprine (Flexeril) 5-10 tid (a TCA)
- Avoid:
  - Dantrolene (Dantrium) - liver problems
  - Carisoprodol (Soma) - addictive

Opioid Alternatives: α-2-δ Anticonvulsants

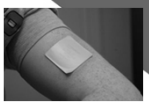
- Work by calming down pain nerves
- Once believed to take 3-6 wks to work, but found to be quite effective in pre-emptive analgesia
- Gabapentin 900-1800/d (tid or qhs)
- Pregabalin 300-450/d (bid or qhs)



- Renal elimination: if ↓ GFR,↓ dose
- ADRs: drowsy, visual, edema, weight gain

- If planning surgery, best to start 3-7 days preop

Opioid Alternatives: Topicals



- Work best for superficial pathology
- NOTE: occlusive seal ↑ absorption 10-40 x!

- Lidocaine (Lidoderm)
- NSAIDs (Voltaren patch/gel/liquid, Flector patch)
- Capsaicin (mostly OTC, except Zostrix)
- Salicylates (OTC: “BenGay”)
- Compounded (Rx: mix of multiple meds)

- Advantages: lack of systemic ADRs
- Disadvantages: $$$, often limited benefit, poss. messy

Alternatives to Opioids in Acute Pain
Physical Therapy

- Thermal
- Electrical (esp. TENS)
- Mechanical traction
- Phoresis
- Bracing
- Exercise
- Manual treatments (stretch, massage, trigger points, etc.)

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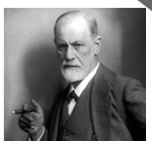
Opioid Alternatives: Behavioral



- ➢Distraction: ↑ desc. inhibition at dorsal horn
- CBT: proven beneficial (esp. for poor copers)
- Stress-reducing mindfulness meditation: may provide similar benefit
- Hypnosis: effective if patient susceptible

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Alternatives to Opioids in Acute Pain
Integrative Medicine

- Manipulation: chiro, osteo, PT, nurse
- Energy Medicine: therapeutic touch, Reiki, homeopathy, etc.
- Physical modalities: massage, yoga, tai chi, qi gong, etc.
- Acupuncture, acupressure, suction
- Music, light, aromatherapy
- Prolotherapy

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Alternatives to Opioids in Acute Pain
Interventional

- Trigger point/muscle injections
- Joint/bursa injections
- Hematoma block (for Colles Fx)

- ➢ Spinal/peripheral stimulators
- ➢ Regional (peripheral nerve) blocks or infusions
- ➢ Epidural blocks or infusions (poss. high)
- ➢ Spinal blocks or infusions

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Alternatives to Opioids in Acute Pain
Pre-emptive analgesia

May include any/all, depending on surgery:

- Preoperative
  - Celecoxib, gabapentinoid, APAP, steroids
- Intraoperative
  - Incisional block, regional block, ketamine
- Postoperative
  - Celecoxib, gabapentinoid, α blockers, APAP, regional/spinal/epidural block

Check out: www.postoppain.org

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Alternatives to Opioids in Acute Pain
Effects of pre-emptive analgesia

- Dramatic reduction in opioid need
  - Many patients get by without using any
- Better compliance with PT/rehab
- Better overall outcomes
- Data on shorter LOS mixed
- Markedly improved HCAHPS Scores

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Specific Tx Considerations: Buprenorphine

- Preop: Don't D/C as outpt; patient may relapse
- Splitting dose into bid-tid may meet pain needs w/o other opioids (may need 8 mg qid)
- Consider injectable buprenorphine (Buprenex) to increase effectiveness
- Can overcome blockade with IV fentanyl, but patient must be monitored (pulse ox, end-tidal CO_2, telemetry bed strongly recommended)
  - Must have ventilatory support and Narcan immediately available

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Specific Tx Considerations: Naltrexone

- May D/C if short-acting, BUT: ↓ opioid blockade over 24-48 hrs. requires constant monitoring and ↓ opioid dosing, or it can lead to OD
  - If done preop as outpatient, may lead to relapse
- Window between overcoming blockade with fentanyl and causing apnea is very narrow
  - Must be in a monitored bed, preferably telemetry
  - Must have ventilatory support and Narcan immediately available
- If at wit's end, call Alkermes at 888-235-8008

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Specific Tx Considerations: Methadone

- Split daily MAT dose into tid-qid oral dosing (will probably meet pain needs w/o using other opioids)
- Can augment with other opioids, but typically will be very tolerant; may need (very) large doses
- Watch out for respiratory depressants (benzos)
- Check drug interactions – very easy to block methadone's metabolism, causing OD
- Check QTc's

Key Points

- Contact addiction Tx center and continue MAT
  - If on buprenorphine or methadone, split dose to tid-qid
- Use APAP, celecoxib (or IV ketorolac), an α-2-δ agent, and a topical if appropriate.
- Consider a nerve block or epidural/spinal
- Consider PT, behavioral, or integrative Tx
- Use pre-emptive analgesia for surgery
- If you must overcome bup/NTX block, use fentanyl and do it in a monitored bed
- ↑↑ pain could indicate a complication or a relapse.
- Avoid writing an opioid Rx for outpatient use unless recommended to do so by consulting addiction treatment provider

Thank you for your time and attention!

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