

Hospital Care of the Narcotic Addict

JoAn Laes, MD

- Division of Addiction Medicine, Hennepin County Medical Center, Minneapolis, MN

Timothy Wiegand, MD

- Director of Medical Toxicology and Toxicology Consult Service, URMC and Strong Memorial Hospital, Rochester, NY

NYSAM

“Intersection of Science, Treatment and Policy”

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Disclosures

- None

Learning Objectives

- Describe options used to treat **opioid withdrawal** in the Emergency Department and Hospital Setting
- Describe the **3-day emergency rule** related to non-x waiver emergency use for the treatment of opioid dependence related to use of buprenorphine
- Describe process of **ED and hospital induction** using buprenorphine and linkage to an outpatient or inpatient treatment program through case-based examples.
- Describe treatment of **pain** in the emergency setting for patients maintained on buprenorphine or naltrexone.
- Describe how **methadone maintenance** affects clinical care related to opioid dependence for patients in methadone maintenance programs seen in the ED or hospital setting.

My Practice....

- Primary specialty: internal medicine
- Sub-specialty: medical toxicology, addiction medicine
 - Addiction Medicine
 - Inpatient consultation
 - emergency department/med-surg/psychiatric inpatients
 - Outpatient consultation
 - Methadone clinic program physician (OTP attached to the hospital)
 - Medical director for detox
 - Medical Toxicology
 - Inpatient and outpatient consultation

Inpatient Addiction Medicine Consults

500 bed urban hospital

Physician/APP/Licensed Alcohol and
Drug Counselors

During a 1 month period:

Physician/APP consults

60 unique patients

total ~100 visits

LADC

2-3x

- Primary substance used
 - Alcohol (~43%)
 - Opioids (33%)
 - Stimulants (2%)
 - Cannabis/cannabinoids (2%)
 - Sedative-hypnotics (1%)
- Consult reason
 - Pharmacotherapy services
 - Alcohol use disorder: naltrexone or acamprosate (64%)
 - Opioid use disorder: buprenorphine or methadone (23%)
 - Withdrawal management
 - Opioid withdrawal (35%)
 - Alcohol withdrawal (2%)
 - Sedative-Hypnotic Withdrawal (2%)

Your Practice...

- Primary Specialties

- Internal Medicine
- Family Medicine
- Psychiatry
- Emergency Medicine
- Anesthesia
- Other

- Sub specialties

- Addiction medicine
- Toxicology
- Pain

Case 1

- 27 year-old opioid dependent M with intravenous opioid use (IVOU) is admitted to the hospital with cellulitis and abscess.
- He is started on IV antibiotics with incision and drainage of an antecubital abscess.
- Ibuprofen 800 mg and APAP 650 mg are administered for pain.
- He is becoming increasingly irritable through the day and requesting more pain medication.

What are the signs and symptoms of opioid withdrawal and what tools are available for evaluation?

Clinical Opiate Withdrawal Scale (COWS)

1) Resting Pulse Rate: Record Beats per Minute		6.) GI Upset: Over Last 1/2 Hour	
0 = pulse rate < 80	2 = pulse rate 101-120	0 = no GI symptoms	3 = vomiting or diarrhea
1 = pulse rate 81-100	4 = pulse rate > 120	1 = stomach cramps	4 = multiple episodes of diarrhea or vomiting
2) Sweating: Over Past 1/2 hour not Accounted for by Room Temperature or Patient Activity		7.) Tremor Observation of Outstretched Hands	
0 = no report chills or flushing	3 = beads of sweat on brow or face	0 = no tremor	2 = slight tremor observable
1 = subjective reports chills/flushing	4 = sweat streaming off face	1 = tremor can be felt, but not observed	4 = gross tremor or muscle twitching
2 = flushed or observable moistness on face			
3) Restlessness Observation During Assessment		8.) Yawning Observation During Assessment	
0 = able to sit still	3 = frequent shifting or extraneous movements of arms/legs	0 = no yawning	2 = yawning 3 or more times during assessment
1 = reports difficulty sitting still but is able to do so	4 = Unable to sit still for more than a few seconds	1 = yawning once or twice during assessment	4 = yawning several times/minute
4) Bone or Joint Aches if Patient was Having Pain Previously only the Additional Component Attributed to Opiate Withdrawal is Scored		9.) Anxiety or Irritability	
0 = not present	2 = patient reports severe diffuse aching of joints/muscles	0 = none	2 = patient obviously irritable/anxious
1 = mild diffuse discomfort	4 = patient is rubbing joints or muscles and is unable to sit still because of discomfort	1 = patient reports increasing irritability or anxiousness	4 = patient so irritable that participation in the assessment is difficult
5) Runny Nose or Tearing Not Accounted for by Cold Symptoms of Allergies		10.) Gooseflesh Skin	
0 = not present	2 = nose running or tearing	0 = skin is smooth	5 = prominent piloerection
1 = nasal stuffiness or unusually moist eyes	4 = nose constantly running or tears streaming down cheeks	1 = piloerection of skin can be felt or hairs standing up on arms	

How might opioid withdrawal present differently in an emergency department/hospital setting?

The case....

- 27 yo IVOU with cellulitis and abscess, difficult to control pain
 - Vs: pulse 105 bpm, bp 150/90 mm Hg, RR 22, 98% O2 RA, T 101 F
 - General: irritable, frequently shifting around in bed
 - Pupils: 4mm
 - Respiratory: non-labored
 - CV: regular rhythm
 - Abdomen: frequent bowel sounds, generalized discomfort on palpation
 - Neuro: faint tremor
 - Skin: Moist hairline, clammy hands, hairs standing on end. Dressing over Left antecubital fossa, right antecubital fossa with IV in place (difficult placement reported)
 - Now receiving morphine 2mg IV q4 hr prn

Medical

- Acute Pain
- Infection
- Gastrointestinal illness

Opioid Withdrawal

- Myalgias/Arthralgias
- Sweating, flushing, chills
- N/v/d

Abnormally
difficult to
control pain

Well, that was sort of non-specific...

Now what?

Getting further history

- IV heroin use x 12 months
 - Progressed to 1 gm daily in past few weeks
 - Last use day prior to admission
 - No history of pharmacotherapy or psychosocial treatments for OUD

- Urine Drug Screen
 - Opiate screen positive

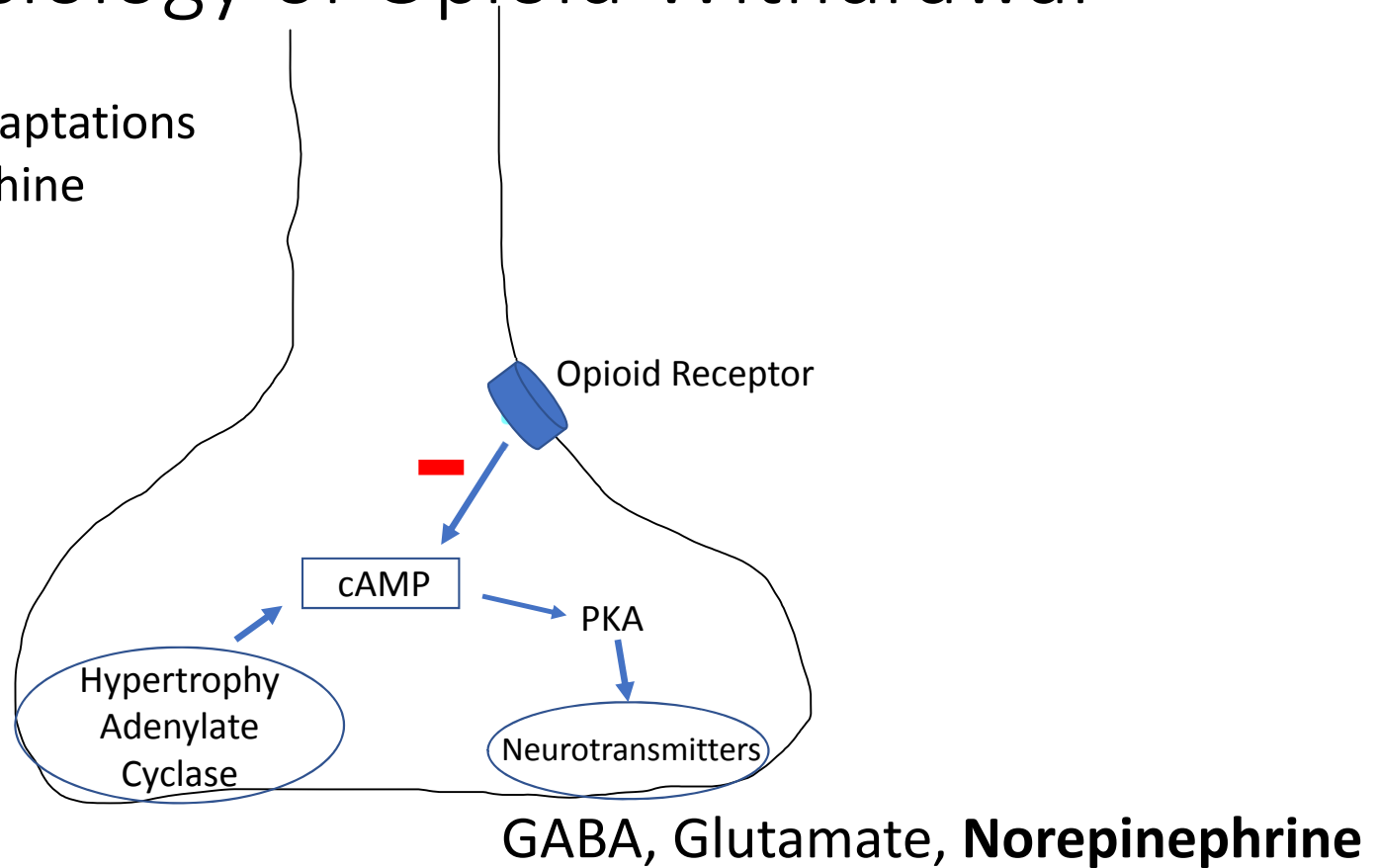
Patient now threatening to leave the hospital due to uncontrolled pain though his infection has not been completely treated.

You assure the patient that you will address his acute medical problems including pain and possible opioid withdrawal symptoms.

What can you recommend?

Pathophysiology of Opioid Withdrawal

Cellular counter adaptations
after chronic morphine



Opioid Withdrawal Management

Opioid Agonists

- Methadone
- Buprenorphine

- Short acting opioids

Non-Opioid Agonists

- Alpha 2 agonists
- GABA promoting agents
- Anti-emetics
- Anti-diarrheals
- Non-opioid analgesia (NSAIDS/APAP)

You decide to use methadone.

You call the pharmacist to confirm the dose for treatment of opioid withdrawal and the pharmacist questions whether it is legal to treat the patient's addiction with methadone in the hospital...

*Sorry pharmacists!

Title 21 Code of Federal Regulations

Section 1306.07 Administering or Dispensing of Narcotic Drugs

(b) Nothing in this section shall prohibit a physician who is not specifically registered to conduct a narcotic treatment program from

administering (but not prescribing) narcotic drugs to a person for the purpose of relieving acute withdrawal symptoms

when necessary while arrangements are being made for referral for treatment. Not more than one day's medication may be administered to the person or for the person's use at one time. Such emergency treatment may be carried out for not more than **three days** and may not be renewed or extended.

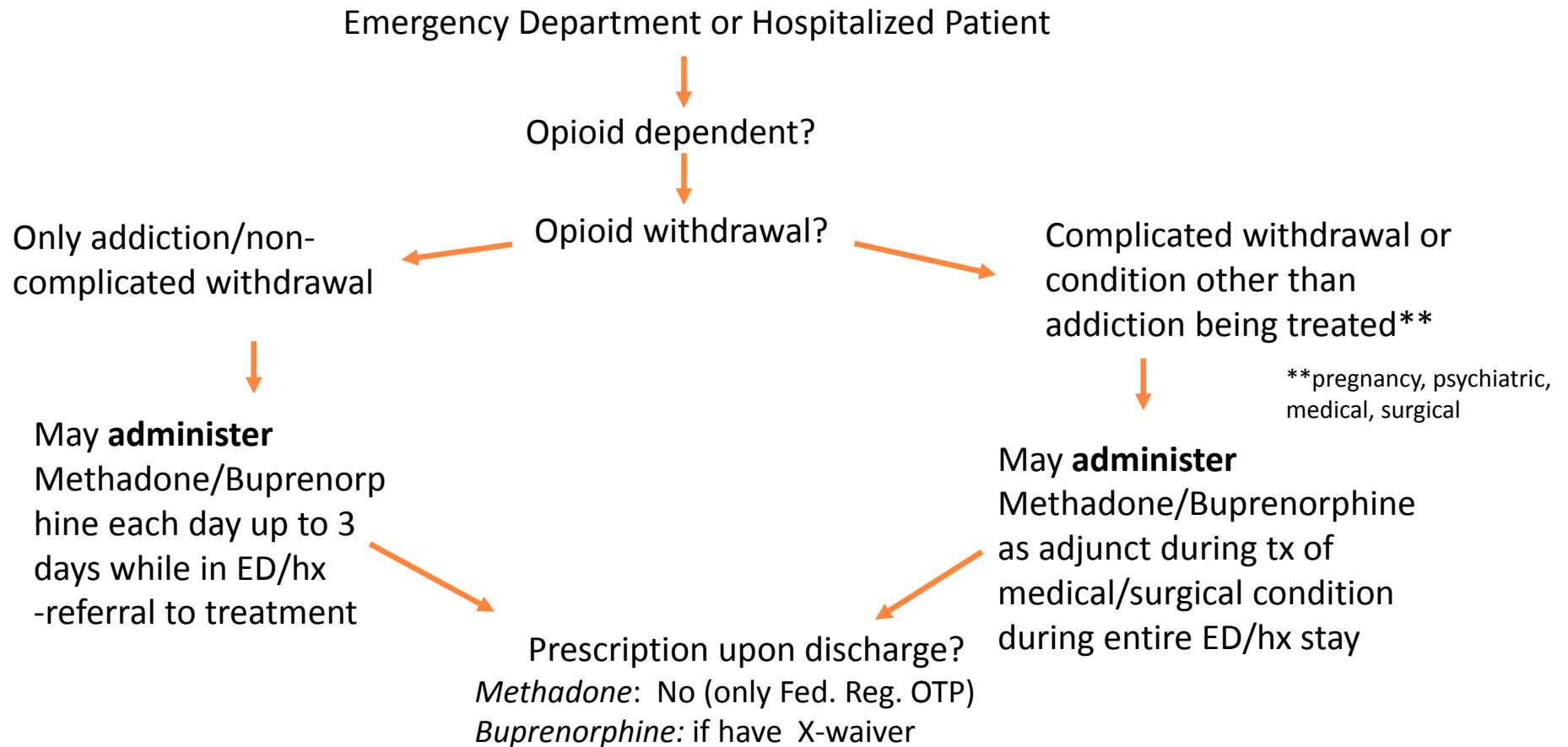
(c) This section is not intended to impose any limitations on a physician or authorized hospital staff to administer or dispense narcotic drugs in a hospital to

maintain or detoxify a person as an incidental adjunct to medical or surgical treatment of conditions

other than addiction, or to administer or dispense narcotic drugs to persons with intractable pain in which no relief or cure is possible or none has been found after reasonable efforts.

Withdrawal Management: Agonists

Title 21 Code of Federal Regulations
Section 1306.07 Administering or Dispensing of Narcotic Drugs



Now back to the dose of methadone...

Withdrawal Management: Methadone



- Various Regimens
 - 5-10mg q4 prn, max 40mg first 24 hours
 - 20-30 mg* daily po
 - *consider 15 mg if history for reduced tolerance or medical risk of respiratory depression
 - 10 mg IM
- For acute pain: supplement short acting analgesia

Withdrawal Management: Methadone

- Treatment Planning
 - Do not discharge with methadone from ED or hospital
 - Outpatient setting limited to federally certified Opioid Treatment Programs
 - Link to Opioid Treatment Program, if available
 - Taper
 - Option for hospitalized patients
 - 3-7 days
 - Many combos: 30 mg /20 mg /**20 mg** or 20 mg/ 20 mg /**15 mg** , etc.

Case 2

- 46 yo F presents to the emergency department (ED) with exacerbated chronic pain and feeling sick due to being cut off from chronic opioid therapy for pain 2 days ago.
 - Provider concerned for misuse of opioid prescriptions
- You take a full history from the patient and determine that she has an opioid use disorder.
- The patient is interested in treating withdrawal and long term medication assisted treatment.

What are the options for the ED?

- Admit to the hospital
 - High risk medical problems: pregnant, severe coronary artery disease, severe electrolyte disturbances
- Prescribe non-opioid agonist medications
- Detox**
- Methadone**
- Buprenorphine + Rx (if X-waivered)**

**Availability of services highly dependent on geographic location, and emergency department policies

Withdrawal Management: Non –Agonist

- **Multiple symptoms**

- **Alpha-2 agonists**

*Clonidine (0.1–0.3 mg PO q 6–8 h) or patch
Guanfacine (1 mg PO tid)*

- **Gaba-ergic**

*Gabapentin (200-600 mg PO tid)
Pregabalin (50 mg PO tid)*

- **Anxiety/restlessness**

- **Benzodiazepines**

*Clonazepam (0.5–2 mg PO q 4–8 h)
Oxazepam (15–30 mg PO q 4–6 h)
Lorazepam (1-2 mg PO, IM, IV)
Diazepam (5-10mg PO/IV q 6-8 h)*

- **Antihistamines**

*Diphenhydramine (50–100 mg PO q 4–6 h)
Hydroxyzine (100–150 mg PO q 6 h)*

- **Beta-blocker***

Propranolol (10 mg PO q8h)

- **Insomnia**

- **Sedating antidepressants**

*Trazodone (50–150 mg PO at hs)
Doxepin (50–100 mg at hs)*

- **Non-benzodiazepine hypnotics**

*Zolpidem (10 mg PO at hs)
Eszopiclone (3 mg PO at hs)*

- **Sedating atypical neuroleptics**

*Quetiapine (50–200 mg PO at hs)
Olanzapine (5 mg PO at hs)*

- **Melatonin**

- **Msk pain**

- **NSAIDs**

*Ibuprofen (400 mg PO q 4–6 h)
Aspirin (650 mg PO q 4–6 h, max 4 g/d)
Ketorolac (30 mg IM q 6 h, max 5d)*

- **Aniline analgesic**

Apap (650–1000 mg PO q 4–6 h)

- **Antispasmodic**

*Cyclobenzaprine (5–10 mg PO q 4–6 h)
Baclofen (5 mg PO tid)
Tizanide (2 mg PO q6-8 h)
Methocarbamol (1000 mg PO qid)*

- **GI Distress (n/v/d)**

- **Oral/IV hydration**

*Sports drinks (electrolytes)
diluted fruit juice
bouillon*

- **Antiemetics**

*Prochlorperazine (5–10 mg PO or IM q 3–4 h)
Promethazine (25 mg PO or IM q 4–6 h)
Ondansetron (8–16 mg PO or IM q 8–12 h)*

- **Antidiarrheal**

Loperamide (2 mg PO after each BM)

- **Miscellaneous**

Bismuth subsalicylate (2 tablets PO q 1 h)

Non-agonist therapies

Alpha-2 agonists

Clonidine (0.1–0.3 mg PO q 6–8 h)

Clonidine 0.1mg/hr patch

Gaba-ergic

Gabapentin (200-600 mg PO tid)

•)

What are the differences in efficacy for agonist vs. non-agonist management of withdrawal?

Withdrawal: Agonists vs Non-agonists

- Buprenorphine for the management of opioid withdrawal, Gowing 2009
 - Cochrane Review
 - Buprenorphine > clonidine:
 - Decrease withdrawal
 - Improve length of time in treatment (particularly outpt)
 - Improve completion withdrawal tx
- Alpha-adrenergic agonists for the management of opioid withdrawal, Gowing 2016
 - Cochrane Review
 - Clonidine >placebo
 - Decreasing withdrawal
 - Completion of treatment
 - Clonidine compared to methadone
 - Clonidine: withdrawal sx occurred earlier and resolved earlier
 - Methadone: Duration of treatment longer
 - Adverse effect with clonidine (hypotension)

How can you facilitate buprenorphine induction in the emergency department?

Buprenorphine-Naloxone in the ED

- Induction in the emergency department
 - 2mg buprenorphine-naloxone sublingual tablet/film → Monitor for withdrawal ~1 hour → 8 mg
 - Other induction options day 1: 4 mg + 4mg or 2mg + 4mg
- Follow-Up
 - Link to treatment (OBOT or OTP) with a maintenance regimen
 - Taper 3-7 days (Rx with X waiver)

Rx Taper Regimen: Buprenorphine

Fixed

- 3 day: (12mg / 8mg /8mg)
- 7 day: (12 mg/8 mg/ 6 mg/ 4 mg/ 4 mg/ 2mg/ 2mg)

Case 2 continues... 46 yo F cut off from chronic opioids

- In reviewing the patients prescription monitoring program, you find this:

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01/23/2017 ALPRAZOLAM 1 MG TABLET 90.00 30 (
12/27/2016 ALPRAZOLAM 1 MG TABLET 90.00 30 (
12/09/2016 ALPRAZOLAM 0.5 MG TABLET 10.00 3
12/01/2016 ALPRAZOLAM 1 MG TABLET 90.00 30 (
12/01/2016 MORPHINE SULFATE IR 15 MG TAB 60.
12/01/2016 MORPHINE SULF ER 30 MG TABLET 60.
11/01/2016 ALPRAZOLAM 1 MG TABLET 90.00 30 (
11/01/2016 ALPRAZOLAM 0.5 MG TABLET 60.00 30
11/01/2016 GABAPENTIN 300 MG CAPSULE 270.00
11/01/2016 MORPHINE SULF ER 30 MG TABLET 60.
11/01/2016 MORPHINE SULFATE IR 15 MG TAB 60.
10/03/2016 ALPRAZOLAM 1 MG TABLET 90.00 30 (
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Issues with Rx Buprenorphine in the Acute Care Setting

- Prior authorization
- Need x waived provider
- Linking to treatment OBOT/OTP
- Emergency department policy
 - Return clientele?
- Concomitant alcohol/sedative hypnotic use

Evaluation of the use of buprenorphine for opioid withdrawal in an emergency department.

Berg et al. 2007

- Retrospective chart review of opioid withdrawal
 - 10 week period, 158 patients
- Buprenorphine (56%), symptomatic tx (26%), no tx (18%)
- No documented adverse outcomes
- repeat drug related visit ED 30 days
 - Buprenorphine (8%)
 - Symptomatic tx (17%)

Linking to OBOT

- 4 studies, 3 randomized
- Compare
 - Buprenorphine plus link to treatment
 - Detox or brief intervention
- Outcomes
 - Buprenorphine
 - Increase treatment entry
 - Retain in treatment longer
 - Reduced illicit drug use
 - Decrease injection opioid use (so did detox)

Linking Buprenorphine from Inpatient to Outpatient

Inpatient initiation of buprenorphine maintenance vs. detoxification: can retention of opioid-dependent patients in outpatient counseling be improved? Caldiero et al. 2006

Retrospective chart review Opioid dependent, treatment	bup induct (30) tramadol taper (30)	<ul style="list-style-type: none"> Remained in outpt tx (bup maintenance 8.5wk: taper 0.4wk)
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Buprenorphine treatment for hospitalized, opioid-dependent patients: a randomized clinical trial.. Liebschutz et al. 2014.

Randomized clinical trial Opioid dependent, hospital	bup w link to OBOT (72) detox (67)	<ul style="list-style-type: none"> Tx entry (bup 72% :detox 12%) Bup at 6 mo (bup 16.7% :detox 3%) Prior 30 day self report illicit (bup incidence ratio 0.60)
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Buprenorphine Initiation and Linkage to Outpatient Buprenorphine do not Reduce Frequency of Injection Opiate Use Following Hospitalization. Cushman et al. 2016

Randomized clinical trial Injection opiate users, hospital	bup linkage (n=51) detox (62)	<ul style="list-style-type: none"> Initial bup visit (70% link : 9.7% detox) No diff. IOU 1,3,6 mo f/u, but dec. compared to grp baseline
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Emergency Department–Initiated Buprenorphine/Naloxone Treatment for Opioid Dependence. D’Onofrio et al. 2015.

Randomized clinical trial Opioid dependent, emergency department	Referral (n=104) brief intervention (n=111) buprenorphine (n=114)	<ul style="list-style-type: none"> Tx at 30 days (bup 78%: brief int. 45%: referral 37%) Days/wk illicit opioid use reduced (bup 4.5: brief int 3.2: referral 3.1) Inpatient addiction services (bup 11%: 35: brief int: 37% referral)
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Case 3

- 27 y/o male with history of IVDU
 - Meds: buprenorphine-naloxone 8mg sl bid for OUD
- Inpatient, Post op day #0 from orthopedic surgery
 - Bupivacaine/fentanyl epidural
- Surgery Team requesting assistance in management of buprenorphine

Published in final edited form as:

Ann Intern Med. 2006 January 17; 144(2): 127–134.

Acute Pain Management for Patients Receiving Maintenance Methadone or Buprenorphine Therapy

Daniel P. Alford, MD, MPH, Peggy Compton, RN, PhD, and Jeffrey H. Samet, MD, MA, MPH
From Boston University Medical Center, Boston, Massachusetts, and University of California, Los Angeles, School of Nursing, Los Angeles, California.

- Methadone
 - Continue maintenance dose
 - Use short acting opioid analgesics, possibly higher dose or frequency, but titrate clinically
- Buprenorphine
 - **1. Continue buprenorphine maintenance therapy and titrate short acting analgesics**
 - 2. Divide buprenorphine dose every 6-8 hours
 - Supplemental dose? 2-4mg
 - 3. Discontinue buprenorphine therapy and use opioid analgesics
 - Convert back to buprenorphine when pain is resolved
 - 4. Discontinue buprenorphine, treat opioid dependence with methadone 20-40mg, and use short acting opioid analgesics to treat pain
 - *inpatient only

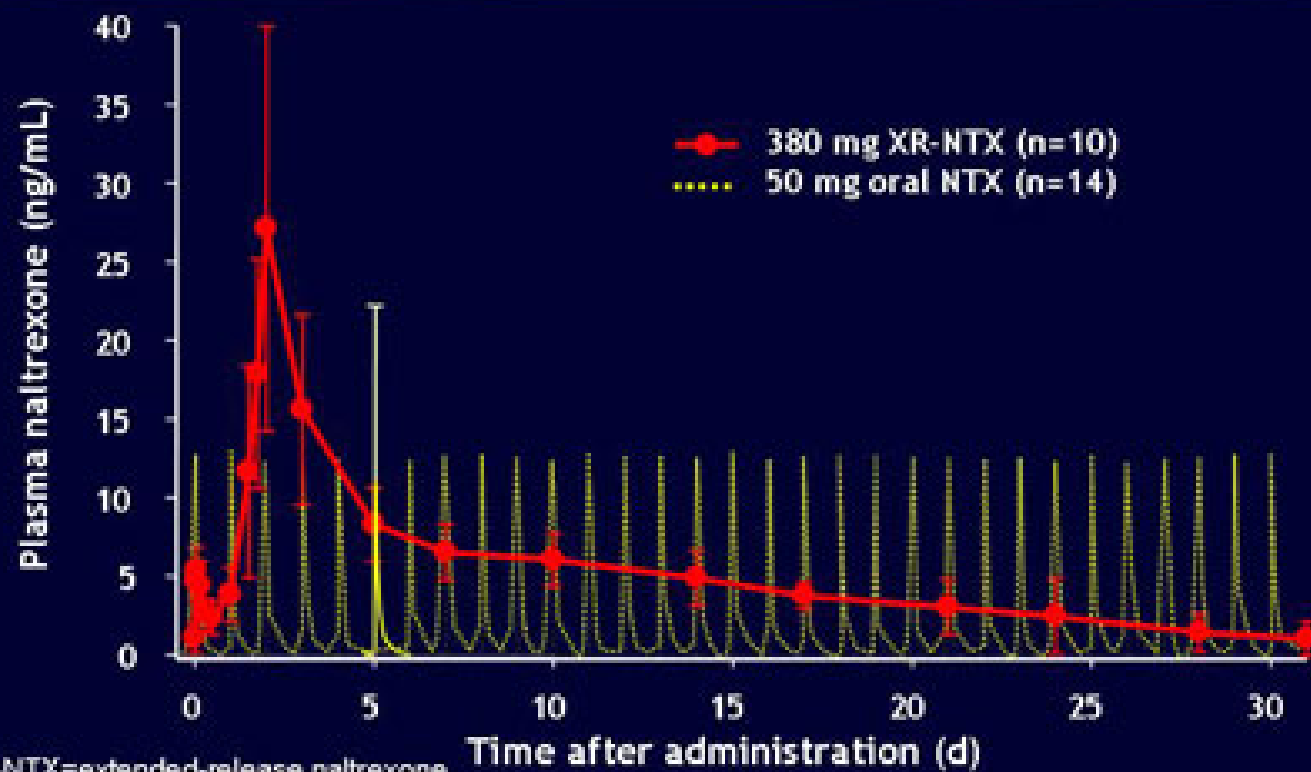
Your plan

- Restart buprenorphine 8mg sl bid on post op day 0 as epidural is being titrated off
- Oxycodone 10-15mg po q4hr prn for pain
 - estimate 1-1.5x typical dosing
 - Adjust clinically as needed
- What if IV management is needed?
 - Fentanyl PCA with a demand dose of anywhere from 25mcg-75mcg Q6-10 min with a RN bolus 100mcg.
 - Ketamine 1mg IV q6-10 minutes as a demand dose with the PCA
 - Continue buprenorphine

Case 4 scenarios

- In a patient treated with naltrexone: what types of options do you have for treating acute and chronic pain?
 - A.) An acute MVA with multiple fractures on po naltrexone?
 - B.) An abscess from an old IVDU attempt that has spread and needs surgical debridement on IM naltrexone?
 - C.) A dislocated shoulder in an alcohol-intoxicated patient?

Injectable Extended-release Naltrexone Maintains a Steady-state Plasma Concentration



XR-NTX=extended-release naltrexone.

Data on file. Alkermes, Inc.
Dean RL. *Front Biosci.* 2005;10:643-655.

Naltrexone Emergency Pain Management

A.) Multiple fractures po naltrexone

- spinal block, general anesthesia
- Ketamine
- If po naltrexone- ?high dose iv opioid such as fentanyl

B.) Abscess, IM naltrexone

- NSAIDS/APAP
- Local Anesthesia

C.) Dislocated shoulder

- Ketamine
- Propofol
- Versed

Case 5

- 28 y/o female with history of OUD on methadone maintenance therapy presenting with altered mental status, fever, and acute low back pain
- You are consulted on the 4th day of admission to assist with methadone maintenance...
- What information do you need?

History for patients on Opiate Agonist Treatment

- Verification of patient's program name and phone number
- Methadone/buprenorphine maintenance dose
- Last face dose of methadone/buprenorphine
- Number of take-outs received on last date in clinic
- Any recent dose changes
- For office based buprenorphine: prescription monitoring programs
- Physical Exam, Laboratory, Diagnostics

Case 5 continues.. 28 yo F with AMS and fever

- History: methadone dose 120 mg, last dose day prior to admission.
- Workup: meningitis and possible lumbar abscess.
- Treatments: hydromorphone 0.4 mg q4 hr. Methadone held due to AMS and concern for aspiration.
- Physical Exam
 - 105 bpm, 145/90 bp, rr 22, 101 F
 - Alert, oriented to name and place, date slightly off, states methadone dose is 200mg
 - Pupils 3 mm
 - Resp: on bipap, keeps attempting to pull mask off to talk to you
 - Skin clammy
 - Abdomen: generalized mild discomfort
 - Decreased strength lower extremities

Management Issues with Patients on Methadone

- Altered mental Status
 - Too much or too little methadone...
- Maintenance dose adjustments
 - Numbers of days missed dosing
 - Presence of condition affecting respiratory drive or causing somnolence
- Acute pain
 - Continue methadone plus provide analgesia
 - *Methadone to morphine: 1-3:1
 - If unable to take PO, consider methadone IV/IM/SQ
 - IV 5- to 10-mg every 8 hours or 2/3 of maintenance dose split bid
- Discharge planning with Opioid Treatment Programs
 - Weekends/holidays

Additional Cases

- Journal of Medical Toxicology March 2016
 - [The New Kid on the Block—Incorporating Buprenorphine into a Medical Toxicology Practice. Timothy J. Wiegand](#)
 - [Case Presentations from the Addiction Academy. JoAn R. Laes, Timothy Wiegand.](#)

Learning Points

- Methadone and buprenorphine can be used in the acute care setting for management of withdrawal
- Non-agonist treatments for withdrawal include clonidine and gabapentin
- Consider continuing buprenorphine for patients with emergent pain conditions
- There are several non-opioid options for treating pain in patients on naltrexone

Thanks and Questions

- Contact information: JoAn.Laes@hcmed.org

Quiz Questions

- A patient with history of intravenous drug use is admitted to the hospital with a myocardial infarction. Methadone is started in the hospital for management of opioid withdrawal symptoms. How long can he be given methadone according to the Title 21 Code of Federal Regulations?
 - A. None, federal regulations don't allow administration of methadone for opioid withdrawal in the hospital
 - B. 72 hours, while setting up referral for substance use disorder treatment
 - C. As long as he is in the hospital being treated for myocardial infarction
 - D. Indefinitely, he may be discharged with a prescription for methadone

Quiz Questions

- Name 3 non-opioid medications that can be used to treat opioid withdrawal

Quiz Question

- What is a typical starting dose of methadone recommended for treatment of withdrawal
 - A. 2mg
 - B. 20mg
 - C. 50mg
 - D. Methadone is not recommended for withdrawal

Special Cases of Opioid Withdrawal

- Tramadol
 - Agonist mu opioid receptor, inhibition of serotonin and norepinephrine reuptake
 - Withdrawal syndrome is atypical and can include the opioid features as well as SNRI type discontinuation effects.
 - Treatment is symptomatic, avoid pro-serotonergic agents
 - Clonidine, benzodiazepines?
- Kratom
 - Herb used in order to alleviate symptoms of opioid withdrawal
 - Abuse and withdrawal less frequently reported
 - Treatment similar to opioid withdrawal syndromes
 - Consider lower doses of opioid agonists?

Additional References/Related Literature

- Mariani JJ, Malcolm RJ, Mamczur AK, Choi JC, Brady R, Nunes E, Levin FR. Pilot trial of gabapentin for the treatment of benzodiazepine abuse or dependence in methadone maintenance patients. *American Journal of Drug and Alcohol Abuse* 2016 Mar 10:1-8. [Epub ahead of print].
- Galbis-Reig D. A Case Report of Kratom Addiction and Withdrawal. *WMJ* 2016 Feb; 115(1): 49-52.
- Giovannitti JA Jr, Thomas SM, Crawford JJ. Alpha-2 adrenergic receptor agonists: a review of current clinical applications. *Anesth Prog* 2015 Spring; 62(1): 31-9.
- Albertson TE, Chenoweth J, Ford J, Owen K, Sutter ME. Is it prime time for alpha-2 adrenoreceptor agonists in the treatment of withdrawal syndromes? *Journal of Medical Toxicology* 2014 Dec; 10(4): 369-81.

Methadone

- Activity at multiple receptor systems:
 - **Mu opioid**/NMDA/5HT/NE
 - Absorption 30 min, Peak 2-4 hours
 - Half life ~30 hrs (30.4 ± 16.3)
 - Highly variable
 - CYP 3A4 (+ 2D6, 1A2, 2C9, 2C19, 2B6) to EDDP (inactive)
 - Genetic polymorphisms
 - Elimination:hepatobiliary/renal

Table 1. Relation Between Signs and Symptoms of Opiate Withdrawal and Initial Methadone Dose

Signs and Symptoms	Initial Methadone Dose
Grade 1: lacrimation, rhinorrhea, diaphoresis, yawning, restlessness, and insomnia	5 mg
Grade 2: dilated pupils, piloerection, muscle twitching, myalgia, arthralgia, and abdominal pain	10 mg
Grade 3: tachycardia, hypertension, tachypnea, fever, anorexia, nausea, and extreme restlessness	15 mg
Grade 4: diarrhea, vomiting, dehydration, hyperglycemia, hypotension, and curled-up position.	20 mg

Guidelines for the Management of Hospitalized Narcotics Addicts

JM Fultz et al. Ann Intern Med 82 (6), 815-818. 6 1975. [more](#)

- Narcotic
 - Medical
 - referring to any psychoactive compound with sleep inducing properties
 - Legal
 - federally prohibited drug such as heroin, cocaine

Any questions about buprenorphine or non-agonist management?

Any further questions on pain management?