

Buprenorphine

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Objectives

- × Appreciate the role and effectiveness of buprenorphine in treating opioid dependence
- × Become familiar with induction and dosing protocols
- × Become familiar with strategies for improved treatment success
- × Appreciate ways to reduce diversion

Buprenorphine Basics

Question 1

× Buprenorphine's neurochemical action is as:

- A. Full mu agonist
- B. Partial mu agonist
- C. Kappa agonist
- D. Kappa antagonist
- E. B and D
- F. B and C

Buprenorphine

- × 2000: Drug Abuse Treatment Act [DATA] made possible office based prescribing of schedule III opioids
- × 2002: FDA approves long acting sublingual buprenorphine as schedule III opioid
- × Drs required to have 8 hour special training and an X number
- × Upto 30 patients 1st year, then may apply to treat upto 100 patients

Buprenorphine

- × High affinity partial mu agonist and kappa antagonist
- × Available as sl strips and tablets
- × Two forms- mono [subutex], and combo [suboxone]: 4/1 ratio of bup:naloxone to reduce IV use
- × Reduced opioid agonist effects, ceiling at 24-32 mg; less respiratory suppression
- × Half life 37 hrs
- × Dosing 8-32mg/d
- × Can precipitate withdrawal
- × Absorption (poor oral)
- × Metabolized by CYP 3A4 system

Benefits of Office-Based Treatment

- Private, confidential, and safe treatment provided in a doctor's office
- Allows for continuity of care with primary physician
- Does not require daily visits to a clinic or out-of-town, costly residential treatment
- May allow more patient time for work, family and other activities
- ✕ Improved access

Effectiveness- comparison with methadone

Question 2

× Compared to high dose methadone, buprenorphine has:

- A. Higher treatment retention rates
- B. Lower treatment retention rates
- C. Equal rates of opioid free urines
- D. A and C
- E. B and C

Opioid urine results

- N=225 Randomly assigned, double-blind
- Mean Opioid Free Scores Over 1st 26 Weeks
 - 8mg/day buprenorphine = 44.6%
 - 30 mg/day methadone = 44.5%
 - 80mg/day methadone = 61.9%

Cochrane Review

- × Meta analysis of 8 studies through 2006
- × N = 1068
- × Methadone more likely than bup to retain patients
[RR 0.85; 95% CI 0.73-0.98]
- × No significant differences in opioid use by UA
- × [Mattick et al., 2008]

Induction and Dosing

Question 3

✕ In a major study, at 8 week follow up post 16 weeks of buprenorphine treatment, relapse rates were approximately:

- A. 30%
- B. 50%
- C. 70%
- D. 80%
- E. 90%

Assessing for treatment

- × Diagnosis of opioid dependence
- × Does patient want treatment?
- × Does patient understand risks/benefits?
- × Can patient be expected to be compliant?
- × Can patient follow safety procedures?
- × Psychiatric stability
- × Psychosocial stability
- × Use of alcohol/benzodiazepines
- × Office resources

Preparing for treatment

- × H&P
- × Labwork [LFTs, HIV, hepatitis panel]
- × UDS
- × Patient education
- × Consent for treatment and treatment agreement
- × Check PMP
- × Arrange psychosocial treatment
- × Consider family involvement
- × **USE combination pill for induction, unless pregnant or documented allergy to NTX**

Induction: home vs office based!

- × Tip 40 allowed for office based induction only
- × However, recent studies have shown potential safety of home based inductions
- × No difference in completion of induction [Alford et al., 2007]
- × Cunningham et al., JSAT 2011, 40: 349-356
 - × 84% chose home based induction
 - × NO significant difference in opioid use
 - × GREATER reductions in any drug use

In office induction- day 1

- × Instruct patients to abstain for 12-24 hours [48-72 hours if switching from methadone]
- × Arrange transport home
- × COWS of greater than or equal to 12 [withdrawal]
- × 1st dose 4 mg bup/ntx
- × Reassess 1 hour
- × Ok to give another dose if still in withdrawal
- × General max dose 1st day: 8-12 mg

In-office induction day 2-3

- × Phone contact ok
- × Assess how patient did
- × OK to increase dose by 4 mg if previous day's dose inadequate

Home induction

- × Lee et al., Gen Int Med 24: 226-232 [2008]
 - × Upto 12 mg on day 1
 - × 73% completed week 1
 - × 5% had mild-moderate precipitated withdrawal
 - × 8% had unrelieved prolonged withdrawal [21% who were switching from methadone]
 - × Pts with withdrawal just as likely to follow up at week 1

Home Induction

- × Teach proper administration
- × Teach what symptoms of withdrawals are
- × Prescribe only 1 week supply at 16 mg max dose
- × Pt monitors for withdrawal
- × When in withdrawal, self-administers 4 mg
- × May repeat q 1 hrs until total max dose of 12 mg on day 1
- × On day 2, phone contact, and may go upto 16 mg

Switch from methadone

- × CANNOT recommend switching from a high dose of methadone
- × Wait until methadone dose 30 mg or less
- × Wait at least 48 [usually 72 hours] before attempting bup/ntx induction

Induction Trouble shooting

- × If pt not in withdrawal, generally safest to provide adjunctive meds and re-assess next day
- × Precipitated withdrawal:
 - × Stop and give comfort meds
 - × **Continue on with induction**- additional dose is not likely to worsen withdrawals, plus it may protect patient in case they use illicit opiates through greater mu receptor blockade, bup will take over after about 3 hours

Maintenance

- × ONCE daily dose in most cases when using for addictions
- × Doses greater than 16 mg rarely indicated
- × 16 mg bup decreased mu opioid availability by 85-92%, and 32 mg decreased it by 94-98% [Greenwald et al., Neuropsychopharm 28: 2000-2009; 2003]

Maintenance

- × No ideal duration of treatment
- × However, if high doses utilized, try to reduce to a target dose of 16 mg after 6 months of tx

Other tips

- × No more than 2 tabs/strips at once under the tongue
- × Pregnancy test monthly
- × If pregnant, switch to buprenorphine mono-product
- × UDS initially weekly, but at least monthly
- × PMP monitoring
- × Counseling!! [MI, network therapy, drug counseling, CBT, 12 step]
- × Collaboration of care
- × Treatment of co-occurring illnesses

In case of positive drug screens

- × Do not D/c treatment in case of 1, or even several positive urine drug screens
- × Increase intensity/frequency of counseling
- × Reduction in take home doses
- × Raising the dose if ongoing opioid use
- × Consider switching to higher structure- OTP, methadone

“ Detoxification from heroin is good for many things – but staying off heroin is not one of them”

Walter Ling

Minimizing diversion

Question 4

× All of the following have been found to predict misuse of buprenorphine **except**:

- A. History of injection drug use
- B. History of post traumatic stress disorder [PTSD]
- C. Perceived inadequate dose of buprenorphine
- D. Unstable living situation
- E. Cannabis use

Strategies to minimize diversion

- × Is the person appropriate for office based treatment?
- × Open discussion of diversion concerns
- × Treatment agreement
- × UDS randomly
- × PMP monitoring
- × Counseling weekly
- × Initial weekly scripts-increase to monthly as patient does well
- × Use a therapeutic dose
- × Random pill counts
- × Enlist aid of pharmacists!!
- × Consider lock boxes
- × Contingency management principles

Challenges and strengths faced by our IHS providers

- × Resources
- × Confidentiality
- × Staffing
- × Electronic health record system
- × Possibilities for collaboration of care
- × Example: Cherokee Indian Hospital, North Carolina

What Next

- × Obtain waiver!
- × Ongoing education and training
- × Educating/training clinic staff and administration

Training Resources

- × PCSS B: <http://www.pcspb.org/> training and mentoring program focused on increasing access to treatment for opioid dependent patients.
- × PCSS O: <http://www.pcso.org/> mentoring, webinars
- × PCSS-B has patient/family information, screening forms, tx agreements, 42 CFR compliant consent forms, COWS

Summary

- × Buprenorphine is an effective medication for treatment of opioid dependence
- × The combination product of buprenorphine/naloxone should be used with the exceptions of pregnancy and allergy to naltrexone in order to minimize diversion
- × Close monitoring is necessary during induction, but does not have to be done in person
- × With judicious selection, many patients can be induced on the medication at home
- × While there is no one right dose for everyone, doses of 16 mg and under should be used in a majority of cases

Summary

- × Counseling and psychosocial treatments are an essential part of treatment
- × Collaboration of care with other physicians and pharmacists is necessary
- × Management of diversion must be a part of a comprehensive treatment plan