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

- 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 1\textsuperscript{st} 26 Weeks**
  - 8mg/day buprenorphine = 44.6%
  - 30 mg/day methadone = 44.5%
  - 80mg/day methadone = 61.9%

*Ling et al., 1996*
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.pcssb.org/](http://www.pcssb.org/) training and mentoring program focused on increasing access to treatment for opioid dependent patients.
- PCSS O: [http://www.pcss-o.org/](http://www.pcss-o.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