ECHO Idaho: Opioid Addiction and Treatment
TeleECHO™ Session

Buprenorphine/Suboxone Basics

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The speaker has no significant financial conflicts of interest to disclose.
Learning Objectives

1) Become familiar with the pharmacological characteristics of Buprenorphine/Suboxone
2) Become familiar with the indications and concerns around using Buprenorphine/Suboxone
3) Learn general concepts in the clinical use of Buprenorphine/Suboxone
4) Become familiar with differences and similarities between Buprenorphine/Suboxone and Methadone.
Origin of Buprenorphine Treatment

• Methadone clinics started in 1974. Highly regulated at the federal level. Physicians cannot prescribe methadone outside of a methadone clinics for opioid maintenance.

• Need for access to care for opioid addiction led to data 2000. This was the Drug Addiction Treatment Act of 2000 which allowed physicians to prescribe certain narcotic drugs for maintenance treatment or detoxification treatment.

• But, there are certain requirement, ie. Take course.

• Max 30 patients in first year, 100 after that but must report that are doing so.

• Provider must endorse that they have the capacity to refer patients for appropriate counseling and ancillary services.
Buprenorphine characteristics

- Opioid partial agonist
- High affinity for Mu receptor, therefore displacing full Mu agonist like heroine or methadone.
- Disassociates from the Mu receptor slowly therefore blocking other opioids from the receptor
Buprenorphine is a Partial Agonist

![Graph showing the effects of different drug doses on mu receptor intrinsic activity.](Graph showing the effects of different drug doses on mu receptor intrinsic activity.)

- **Full Agonist**: e.g. heroin
- **Partial Agonist**: e.g. buprenorphine
- **Antagonist**: e.g. naloxone

Buprenorphine does not fully activate mu receptors even with high doses.
Pharmacology of Full vs. Partial Agonists

- Buprenorphine can precipitate withdrawal if it displaces a full agonist from the mu receptors.
- Buprenorphine only partially activates the receptors; therefore, a net decrease in activation occurs and withdrawal develops.

A Net Decrease in Receptor Activity if a Partial Agonist displaces Full Agonist
Suboxone (Buprenorphine/Naloxone)

- Naloxone is 100 times more potent when injected versus taken sublingually. So if injected receptors get blocked, but SL, not enough Naloxone effect to significantly interfere with Buprenorphine.
- Also, Buprenorphine is given SL because it has poor bioavailability if given PO.
- Subutex is Buprenorphine only. Used in pregnancy. Has more diversion potential than the bup/nx combination; hence, the combination is the recommended form for treatment of opioid addiction except in pregnant, opioid dependent, women
Formulations of Buprenorphine

- Parenteral form for treatment of moderate to severe pain (not approved for opioid dependence treatment)
- 7-day Transdermal Patch (5, 10, and 20 µg/hour) for severe pain
- Sublingual forms (tablets and films) for treatment of opioid addiction; not approved for pain management
- Implant now in clinical trials for treatment of opioid addiction
- Buprenorphine/naloxone film (FDA approved 8/31/10) Equivalent in strength to tablets. Dissolves more rapidly (5-6 min) than tablets. Participants in clinical trials preferred taste over that of tablets. Childproof foil packet improves safety of product
- Buprenorphine/naloxone tablets are now available as generic medications
Side effects

• Nausea/vomiting (consider precipitated withdrawal)
• Constipation
• Sedation (use of other sedating drugs or in those not currently dependent, but eligible for buprenorphine treatment by history)
• Transient elevations in liver transaminases possible (Hep C at higher risk)
• Headaches
Adverse effects, concerns, and advantages

• Overdose and deaths, but some protection when taken alone because of partial agonist properties.
• Lack of tolerance
• Higher risk when combined with some other drugs substance (BENZOS, ETOH, other sedative-hypnotics, muscle relaxants).
• Diversion risk
• Lower risk than methadone of arrythmias, (QT prolongations and Torsads)
• Minimal subjective effects when used sublingually: clearheaded, improved energy/sleep
• Hepatic disease
• Pregnancy
• Seizure disorders
• HIV
Efficacy

• Trials reliably demonstrated efficacy in preventing relapse to heroin:
  • Buprenorphine is more effective than placebo.
  • Buprenorphine is equally effective as moderate doses of methadone (e.g.: < 60 mg per day) with respect to treatment retention (59% at 6 months; Stein et al. 2005)
  • At higher methadone doses ( > 60 mg/day), treatment retention increases to 80% (Hser et al., 2014)
Different Doses of Buprenorphine: Opiate Use Decreases with Increased Dose of Buprenorphine
Buprenorphine – Methadone: Opioid Urine Results are Similar: Fewer Opioid Positive Urine with Treatment
### Buprenorphine – Methadone Comparison

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<thead>
<tr>
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<th>Buprenorphine</th>
<th>Methadone</th>
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<tbody>
<tr>
<td><strong>Regulation/Diversion</strong></td>
<td>Partial agonist</td>
<td>Full agonist</td>
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<td>May be diverted</td>
<td>May be diverted</td>
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<tr>
<td></td>
<td>Less regulation</td>
<td>Toxicity risk greater</td>
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<td></td>
<td>Can be used in office-based treatment of opioid dependence</td>
<td>Specialized centers required for treatment of opioid dependence</td>
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<td><strong>Dose/side Effects</strong></td>
<td>Preferred is combo: bup/nlx</td>
<td>Relatively high dose required for tolerance induction; continued opiate</td>
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<td>Fewer side effects</td>
<td>effects, sedation</td>
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<td></td>
<td>Precipitated withdrawal potential</td>
<td></td>
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<td>Reduced risk of overdose</td>
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<td><strong>Ease of Use</strong></td>
<td>Induction generally requires clinical monitoring</td>
<td>Induction and dosing straightforward first doses should be monitored</td>
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<td>Available by prescription</td>
<td>Withdrawal challenging; Complaints of significant discomfort</td>
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<td>Withdrawal better tolerated</td>
<td>Risk of ventricular arrhythmias</td>
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<td>Favorable side effect profile</td>
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<td><strong>Drug Interactions</strong></td>
<td>No clinically significant with HIV meds except atazanavir; rifampin assoc. with</td>
<td>Numerous, especially HIV meds, TB</td>
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<td>withdrawal; BZD (particularly injected) and CNS depressants a concern</td>
<td>meds, some anticonvulsants; concern about interactions with BZDs and other</td>
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<td>CNS depressants</td>
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Clinical use

• Induction
  – Long verses short acting opiates
  – Reduce methadone dose
  – COWS >8
  – Ancillary meds (esp. with methadone)?
  – Home induction?
  – Patients not physically dependent

• Stabilization

• Maintenance
  – How long?

• Withdrawal
  – As primary treatment or termination of maintenance therapy
  – Ancillary meds
Summary

• Induction
  – Long versus short acting opiates
  – Reduce methadone dose
  – COWS >8
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