Understanding Buprenorphine Formulations and Clinical Guidelines for Use

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Monday, March 16th, 2020
The use of affirming language inspires hope and advances recovery.

LANGUAGE MATTERS.

Words have power.

PEOPLE FIRST.

The ATTC Network uses affirming language to promote the promises of recovery by advancing evidence-based and culturally informed practices.
Overview

• Current U.S. opioid epidemic
  – Trends in opioid use, overdose deaths
• Introduction to treatment approaches
• Consumer perspective
• Buprenorphine formulations
• Choosing the most appropriate formulation
• Questions and discussion
The Opioid Epidemic

Source: Centers for Disease Control
Oxycodone consumption, mg/capita

Despite a decline in recent years, U.S. per capita opioid consumption remains much higher than oxycodone consumption in Europe.

Source: The International Narcotics Control Board
Nonmedical Opioid Use and Overdose: Epidemiology

• 4 in 5 new heroin users started out misusing prescription painkillers. As a consequence, the rate of heroin overdose deaths nearly quadrupled from 2000 to 2013.

• In 2017, the number of opioid-related overdose deaths was 6 times higher than in 1999.

• 2017 overdose rates CDC: 70,237 drug overdose deaths in U.S., over 2/3 linked to opioids
  – 45% increase in fentanyl ( & analog)-related deaths since 2016

CDC 2018; 2014 NSDUH, Hedegaard MD et al, 2015
Opioid Use Disorder Treatment Approaches

- **Withdrawal management:**
  - Opioid-based (methadone, buprenorphine)
  - Non-opioid based (clonidine, supportive meds)

- **Maintenance tx/relapse prevention:**
  - Agonist maintenance (methadone)
  - Partial agonist maintenance (buprenorphine)
  - Antagonist maintenance (naltrexone)

- **Psychosocial treatment**
  - Behavioral approaches/skills
Opioid Withdrawal Management (i.e. “detox”)

Medications used to alleviate withdrawal symptoms:
- Opioid agonists (methadone, buprenorphine)
- Clonidine, lofexidine (alpha-2 agonists)
- Other supportive meds
  - anti-diarrheals, anti-emetics, ibuprofen, muscle relaxants, BDZs
Why Not Detoxification?

POST-DETOXIFICATION RELAPSE RATES APPROACH 100% WITHIN THE FIRST 90 DAYS FOLLOWING COMPLETION OF DETOXIFICATION.
MAINTENANCE VS. TAPER: RETENTION

![Graph showing maintenance vs. taper retention over treatment duration in days. The x-axis represents treatment duration in days, ranging from 0 to 350. The y-axis represents remaining in treatment, with values from 0 to 20. The graph compares detox/placebo (green squares) and buprenorphine (red circles).]
# MAINTENANCE VS. TAPER: MORTALITY

<table>
<thead>
<tr>
<th></th>
<th>Detox/Placebo</th>
<th>Buprenorphine</th>
<th>Cox regression</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dead</strong></td>
<td>4/20 (20%)</td>
<td>0/20 (0%)</td>
<td>$\chi^2=5.9$; $p=0.015$</td>
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Buprenorphine
Transmucosal Buprenorphine Formulations

- Sublingual dose: 2mg-24mg/day
- Subutex (buprenorphine) (2mg, 8mg)
- Suboxone (4:1 bup:naloxone)
  - 2mg/0.5 mg, 8mg/2mg
  - (now also in 4mg/12mg)
- Zubsolv (4:1 bup:naloxone)
  - (1.4/0.36mg- 11.4/2.9mg)
- Bunavail (6:1 buccal film bup:naloxone)
  - (2.1/0.3mg, 4.2/0.7mg, 6.3/1mg)
- Belbuca (75-900mcg buccal film for pain)
Buprenorphine for Opioid Use Disorder

- FDA approved 2002, age 16+
- Mandatory certification from DEA (100 pt. limit)
- Mechanism: partial mu agonist
- Office-based, expands availability
- Analgesic properties
- Ceiling effect
- Lower abuse potential
- Safer in overdose
Buprenorphine: Pharmacological Characteristics

Partial Agonist (ceiling effect)
- less euphoria
- safer in overdose

Strong Receptor Binding
- long duration of action
- 1st dose given during withdrawal
Fentanyl vs. Buprenorphine

Dahan et al., 2006
Buprenorphine Implant: Probuphine

- Probuphine™ is an implantable formulation of buprenorphine HCL (80 mg) approved for the treatment of opioid use disorder in patients stabilized on 8 mg/day or less sublingual buprenorphine.
- Probuphine is inserted subdermally into the inner side of the upper arm in a brief in-office procedure under local anesthetic, and provides sustained release of buprenorphine for 6 months.
  - At the end of each 6-month period, Probuphine is removed in a brief, in-office procedure.
Buprenorphone Injection: Sublocade

• Sublocade is a monthly injectable formulation of buprenorphine approved in 2017 for the treatment of moderate to severe OUD in individuals who have initiated a transmucosal buprenorphine product and have been stabilized on treatment for at least seven days.

• The approved dosing regimen is 300 mg administered subcutaneously for the first two months, followed by maintenance doses of 100 mg/month.

• It must be prescribed as part of a Risk Evaluation and Mitigation Strategy to ensure that the product is not distributed directly to patients.
SL-BUP compared to XR-BUP

Lofwall et al., 2018
Naloxone
Short-acting opioid antagonist

- High affinity for mu opioid receptor
- Displaces opioids from receptor
- Rapidly reverses effects of opioid overdose (minutes)
- Effects last 20-90 mins
- FDA approved for IV, SC, IM, intranasal use

- Opioid overdose-related deaths can be prevented when naloxone is administered in a timely manner.

- PrescribeToPrevent.org
Overdose Risk Factors

• History of prior overdose
  • Release after emergency care for overdose
• Opioid use disorder
• Prescribed more than 50 mg of oral morphine equivalents daily
• Recent release from incarcerated or residential setting
• Combining opioids with other central nervous system depressants (e.g. alcohol, benzos)
• Medical conditions (e.g. pulmonary diseases)
Narcan Now App

What is NARCAN (naloxone HCL) Nasal Spray

NARCAN Nasal Spray is the ONLY FDA-approved Nasal Naloxone for the Emergency Treatment of Opioid Overdose

- Needle-Free
- Ready-to-use
- 4 mg concentrated dose

Please see indications and important safety information below
Find out more:
Step-by-Step Guide
Step-by-Step instructions to show how to use
NARCAN® Nasal Spray

NARCAN® Nasal Spray Presentation Video
Watch video on how to use NARCAN® Nasal Spray in an emergency

Indication and Important Safety Info.
emergency medical care.

IMPORTANT SAFETY INFORMATION
NARCAN® Nasal Spray is contraindicated in patients known to be hypersensitive to naloxone

IDENTIFY OPIOID OVERDOSE
AND CHECK FOR RESPONSE

Ask
person if he or she is okay and shout name

Shake
shoulders and firmly rub the middle of their chest

Check for signs of an opioid overdose:

Will not wake up or respond to your voice or touch
In California, you can obtain NARCAN® Nasal Spray directly from your pharmacist without an individualized physician's prescription.
Factors to Consider in Shared Decisions on Choosing Formulations – Sublingual/Buccal

- The most common dosage form in use
  - All patients must be stabilized on sublingual or buccal preparations prior to switch to injectable or implant
  - Can be administered at home or in the office (e.g., during office-based induction)

- For patients with limited or no insurance, the least expensive option
  - For patients with insurance it may be the only option

- Advantages are cost and flexibility
  - A wide range of doses can be prescribed for a few days or for 30 days with refills

- Disadvantages are the risk of diversion, the potential for drug holidays
  - Wrapper counts at each visit; Urine buprenorphine screening
Factors to Consider in Shared Decisions on Choosing Formulations - Injection

- Less commonly used because it is more recent (approved in 2017) and more logistically challenging
  - Only available from registered pharmacies, must be refrigerated, and can only be administered in the clinic setting

- In California, available at no charge to patients with Medi-Cal

- Covers a wide range of buprenorphine doses (8 to 24 mg daily)

- Advantages over films
  - No need for take medication daily (no lost prescriptions or missed doses); No diversion risk; Lasts for one month

- Disadvantages
  - Injection can be painful and leaves a lump that slowly dissolves over time
Factors to Consider in Shared Decisions on Choosing Formulations - Implant

• Less commonly used
  – Requires additional training (above X-waiver training) to prescribe and insert
  – Insertion is a surgical procedure done under sterile procedures and may be done in a separate location

• Advantages
  – The longest-acting dosage form – 6 months

• Disadvantages
  – Only approved for patients stabilized on buprenorphine doses of 8 mg or less
  – After one insertion in each arm, transition to oral is recommended
  – Procedure to implant is straightforward, but there are risks
Glimmers of Hope?

Change in Overdose Deaths Last Year

Reductions in New England give some cause for hope, while the situation in the Midwest and Mid-Atlantic remains bleak.

Note: These numbers are adjusted to account for some death investigations that are not completed. They may change slightly before they become final. Estimates for less populous states are highly variable.

Source: Centers for Disease Control and Prevention

New York Times August 15, 2018
2018: Reduction in US Overdose Deaths

Questions and Discussion
Thank you!

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PSATTC Post-Event Feedback

ATTC Event Feedback

Please provide post-event feedback here:
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pass=51JG*J*aT&EventCode=4421031620&FU=0