Medication Assisted Treatment for Opioid Use Disorders and Veteran Populations

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Learning Objectives

• Understand how veteran populations are vulnerable to Opioid Use Disorders (OUDs)
• Understand the mechanisms of action buprenorphine, methadone and naltrexone
• Understand the advantages and disadvantages of each medication discussed.
Veterans and Mental Health

- 22 million veterans in the US population
- Vets make up 8.5% of the US population but account for 18% of suicides\(^1\)
- 22 vets die from suicide each day\(^2\)
- Rate of Post Traumatic Stress Disorder (PTSD) in current and former service members is 8%, and 9.2% of all VA users\(^3\)
- PTSD increases the risk of Substance Use Disorders by 3-4 x \(^4\)
- PTSD increases the risk of substance relapse \(^5\)

Veterans and Pain

- High rates of PTSD and pain are common
- True for pre-9/11 vets
- Also true for OIF/OEF vets
- Veterans are more likely than civilian counterparts to have chronic pain\(^6\)
  - 60% recent vets
  - 50% vets overall
  - c/w 30% civilian population with CP
### Veterans and Opioids

- Opioid Rxs increased 270% over 12 years\(^7\)
- OUDs in vets increased 55% \(^8\)
- Vets are 2x likely to become addicted to opioids compared to the civilian population
- Vets are 2x likely to die of overdose compared to the civilian population\(^9\)
- Vets getting opioids 233% more likely to have adverse clinical outcomes\(^{10}\)

### Veterans and Opioids

- Vets with PTSD and pain\(^{10}\)
  - 260% more likely to get opioids
  - 42% more likely to get high dose
  - 87% more likely to get \(\geq 2\) opioids concurrently
  - 546% more likely to get sedatives concurrently
  - 64% more likely to get early refills
Opioid addiction

- Tolerance develops quickly
- Use gets perpetuated by....
- Positive reinforcement
  - Get euphoria (high)
- Negative reinforcement
  - Get withdrawal when wears off
  - Withdrawal is pretty unpleasant

Cycle of Addiction

- Drug Euphoria
  +
- Brain Reward
- Neuroadaptations
- Drug Craving
  -
Medication Assisted Treatment

- Reduce opioid use
- Increase retention in treatment
- Reduce HIV risk behaviors
- Reduce overdose deaths

General Opioid Pharmacology

- Full agonists
  - Bind to the receptor and activate the receptor
  - Increasing doses of the drug produce increasing effects until a maximum effect is achieved
    (receptor is fully activated)
  - Most abused opioids are full agonists
General Opioid Pharmacology

- Partial agonists
  - Bind to the receptor and activate the receptor
  - Increasing the dose does not lead to as great an effect as does increasing the dose of a full agonist-less of a maximal effect is achieved
General Opioid Pharmacology

- Antagonists
  - Bind to the receptor, but don’t activate the receptor
  - Block the receptor from being bound by a full agonist or partial agonist
  - Like putting gum in a lock, or…
Efficacy:

Full Agonist (Methadone)
Partial Agonist (Buprenorphine)
Antagonist (Naloxone)

% Efficacy vs Log Dose of Opioid

- Full Agonist (Methadone)
- Partial Agonist (Buprenorphine)
- Antagonist (Naloxone)
Methadone

- Works on the same receptor (mu opioid receptors) as heroin and other abused opioids
- Can use it to taper people down
  - Build a “chemical staircase” for them to walk down
- Can use it to maintain people as well
  - Put on same dose of methadone as heroin
  - Stops withdrawal
  - Ratchet up dose to way past how much heroin they used
  - Price it out of reach
  - Stops positive and negative reinforcement

Buprenorphine

- High affinity for the mu opioid receptor
  - Competes with other opioids and blocks their effects
  - Prevents positive reinforcement
- Slow dissociation from the mu opioid receptor
  - Prolonged therapeutic effect for opioid dependence treatment
  - Long half life (20-44 hours)
  - Prevents negative reinforcement
Methadone

- Schedule II
- Dispensed at Opioid Treatment Programs
- Staffing and practices directed by Federal law
  - 42 CFR Part 8
- Compared to psychosocial interventions alone
  - Increased treatment retention
  - Decreased opioid use
Buprenorphine

- Schedule III
- Office-Based Opioid Treatment (OBOT)
- DATA 2000
  - Addiction specialist (3 kinds)
  - 8 hour course
- Compared to psychosocial interventions alone
  - Improve treatment retention
  - Reduce opioid use

Buprenorphine Maintenance/Detoxification: Retention

(Kakko et al., 2003)
Naltrexone

- Not a controlled substance
- Any licensed provider can Rx
- Oral or long-acting injection
- Compliance is a problem

Naltrexone

- Antagonist therapy based on the behavioral concept of “extinction”
- Euphoric effects of opioids are blocked
- The repeated lack of reinforcement, gradually result in extinction of opioid use
Naltrexone

- Pure opioid antagonist with good oral absorption
- Occupies mu receptors without activating
- Blocks abused agonist opioid drugs
- Duration of action 24-48 hours for oral formulation, one month if IM
- 1984: FDA approved to treat opioid dependence
- Well tolerated and safe

Effectiveness of Naltrexone

Recent Studies:
- Placebo (25.3%) vs. Long-acting injectable naltrexone (61.9%) – negative urine samples after 48 days
- Higher mean days retained in treatment
- Opioid-free weeks from week 5 to 24 were significantly different between treatment groups (90% naltrexone vs. 35% placebo)
- 50% mean reduction in subjective craving
Methadone vs Buprenorphine

- Patient preference typically decides
- Some studies show they are the same
- Some studies show
  - Methadone retains better
  - Buprenorphine reduces opioid use better
- Cochrane meta-analysis:
  - Methadone retains better
  - Equal at reducing opioid use

Naltrexone vs. Buprenorphine

- 2 studies, one Norwegian, one U.S. based
- Found non-inferiority of depot naltrexone
- U.S. study found higher drop outs in the first week for the naltrexone group
- Consider naltrexone for people who present already detoxed (e.g. from correctional settings or post-detox)
How long?

- No solid empirical evidence to answer
- Guidance from TIP 43 is “at least 2 years”
- Stability in multiple domains of life
  - Social
  - Occupational
  - Family

Integration of MAT

- Despite effectiveness of all MAT, NO MEDICATION has been found to change the behaviors associated with illicit drug use
- Thus, behavioral therapies continue to play a critical role in the recovery process:
  - Repairing family and social relationships
  - Finding positing support networks/recreation
  - Obtaining/maintaining fulfilling employment
  - Addressing co-morbid psychiatric/emotional symptoms
MAT in the VAH

- About 53 MMTP in VA system
- Early on, barriers and facilitators to bup were studied (Gordon et al, 2011)
  - Data from 2006-07
  - Lack of perceived need, lack of provider interest and stigma were barriers
  - Need, provider interest, resources were facilitators
- Buprenorphine growing 300 pts at 27 facilities to 6,147 pts at 118 facilities from 2004-2010 (Olivia et al 2013)

VA Response to Opioid Rx

- VA issued prescribing guidelines in 2010
- Between July 2012 and June 2015, reduced the numbers of vets getting opioids by 115,575 people
- Established the Office of Patient-Centered Care, includes non-opioid and alternative approaches to pain
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3. Institute of Medicine, “Treatment for Posttraumatic Stress Disorder in Military and Veteran Populations: Final Assessment.” June 2014
5. Norman 2007
6. Carolyn Clancy, MD Interim Undersecretary for Health, before the Committee on Veteran’s Affairs, U.S. Senate, March 26 2015

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