Methadone and Naltrexone ER

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Disclosures

Neither I nor my spouse has a relevant financial relationship with a commercial interest to disclose.
Objectives

• Review Full Opioid Agonist Methadone
• Review Full Opioid Antagonist Naltrexone
• Case Examples
Methadone and Naltrexone have a similar pharmacology/similar mechanism of action, but Naltrexone can be administered in a primary care setting

a) True
b) False
Medication Therapy

• Opioid Agonists
  – Full: Methadone (Methadose or Dolophine)
  – Partial: Buprenorphine/Naloxone, Buprenorphine (Suboxone or Subutex)

• Opioid Antagonist
  – Naltrexone ER (Vivitrol)
Pharmacology of Treatments

- Full Agonist (Methadone)
- Partial Agonist (Buprenorphine)
- Antagonist (naltrexone)
Goals of Therapy

• Maximal function
  – Stabilization and normalization of the brain
  – Establishment of durable hedonic tone
  – Engagement in care and recovery
  – Prevention of disease transmission
  – Restoration of health
  – Prevention of death

• Achieve appropriate dosage

• NOT to see how fast a patient can taper off medication
Knowledge Check

Although effective in decreasing illegal opioid use, patients treated with methadone in an OTP are highly impaired.

a) True
b) False
Methadone

- Long acting, full opioid agonist
- Binds to and occupies mu–opioid receptors
- Prevents euphoria from other mu agonists
- Alleviates withdrawal symptoms
- Administered in licensed OTP
Methadone

- Federal law: initial dose 10-30 mg, not to exceed 40 mg in day 1
- Suppresses cravings (60-120mg+)
- Can prolong QTc with risk of Torsades de Pointes
- Respiratory depression can be a side effect at any dose
- Increases overdose risk significantly if mixed with sedative hypnotics and ETOH
Methadone Myths

- Substitutes one addiction for another
- Prevents true recovery
- Should not be used long term
- “Liquid Handcuffs”
- Babies born to mothers treated with Methadone are “addicted”
- Rots teeth
- Damages bones
- Turns people into “zombies”
- Causes overdoses
Methadone Facts

• “Opioid Agonist Therapy:” Medication, or Treatment preferred
  – Reduces drug use
  – Reduces the risk of infectious disease transmission
  – Reduces criminal activity
  – Reduces the risk of overdose
  – Reduces death
  – Increases treatment retention
  – Improves social functioning
  – Cost-effective
  – Safe
Hospitalized Patients

- Initiating methadone in hospital:
  - 82% present for follow-up addiction care

Opioid Agonist Therapy Reduces Recurrence

Opioid Agonists Save Lives

To Taper or to Maintain, That is the Question...

- No question, actually.....
- Longer treatment, better outcomes
- Consistent with chronic disease model
- Think DM, CAD, COPD
- As with any medication – no set limit
- Minimum of 12 months, but better outcomes with longer durations
- Continually reassessed and individualized
Treatment Must Maintained

Rapid Return to Injection Drug Use Following Premature Termination of Methadone Maintenance Treatment

- 28.9% after 1-3 Months
- 45.5% after 4-6 Months
- 57.6% after 7-9 Months
- 72.7% after 10-12 Months
- 82.1% after 10-12 Months

(N = 388 Male Patients)
In 2005, methadone and buprenorphine were included in the WHO Model List of Essential Medicines
Knowledge Check

- Naltrexone ER (Vivitrol) is as effective as oral Naltrexone (Revia) for the treatment of opioid use disorder

- A) True
- B) False
Naltrexone

• Full mu opioid antagonist
• Blocks euphoric effect of mu opioid agonists
• No dependence, no need to wean
• Not scheduled – no special training or license needed
• Reduces relapse rates
Naltrexone

- Will precipitate withdrawal if agonists (full or partial) are occupying mu receptors
- Must be 7-10 days opioid free
- Increased risk of overdose if try to overcome blockade
- Increased risk of overdose end of month or missed dose because of loss of tolerance
- Monthly IM dosing improves adherence,
- Oral naltrexone ineffective
- Substantially less stigma
Naltrexone Side Effects

- Generally well tolerated
- GI upset/vomiting
- Diarrhea
- Headache
- Injection site reactions
- Allergic pneumonitis
Naltrexone

- Caution opioid blockade and pain
- Contraindication if active opioid use or concurrent opioid maintenance
- Caution overdose potential
- Must review with patients, must inform of risk of overdose and set safety plan
Extended Release Naltrexone
• 61% received all six injections
• Strict selection criteria, paid $385-820
• Time to relapse significantly longer in NTX group:
  • 10.5 weeks versus 5.0 weeks (P<0.001)
• Relapse in 43% NTX vs 64% controls (P<0.001)
• No difference between groups after treatment completion

A recent study just showed that naltrexone is as effective as buprenorphine.

• A) True
• B) False
Naltrexone ER Injection

Prior to injecting, tap the syringe to release any air bubbles, then push gently on the plunger until 4 mL of the suspension remains in the syringe. (See Figure F.)

THE SUSPENSION IS NOW READY FOR IMMEDIATE ADMINISTRATION.

1. Administer the suspension by deep intramuscular (IM) injection into a gluteal muscle, alternating buttocks per injection. Remember to aspirate for blood before injection. (See Figure G.)

2. Inject the suspension in a smooth and continuous motion.

3. If blood aspirates or the needle clogs, do not inject. Change to the spare needle provided in the carton and administer into an adjacent site in the same gluteal region, again aspirating for blood before injection. REMITRONE must NOT be given intravenously.

After the injection is administered, cover the needle by pressing the safety sheath against a hard surface using a one-handed motion away from self and others. (See Figure H.)

Activating the safety sheath may cause minimum splatter of fluid that may remain on the needle after injection.

DISPOSE OF USED AND UNUSED ITEMS IN PROPER WASTE CONTAINERS

www.mghcme.org
How to Do a Gluteal Injection

Youtube Naltrexone ER Gluteal Injection
Total time spent...

Preparation 2 minutes, 10 seconds

+ 

Administration 1 minute, 25 seconds

Total Time Spent = 3 minutes, 35 seconds
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Exam</td>
<td>15-25 min</td>
</tr>
<tr>
<td>Pap smear</td>
<td>10-20 min</td>
</tr>
<tr>
<td>Incision and Drainage</td>
<td>15-30 min</td>
</tr>
<tr>
<td>Joint Injections</td>
<td>15-30 min</td>
</tr>
<tr>
<td>Ear irrigations</td>
<td>10-15 min</td>
</tr>
<tr>
<td>Manual Vital Signs</td>
<td>2-4 min</td>
</tr>
<tr>
<td>Immunizations</td>
<td>2-5 min</td>
</tr>
</tbody>
</table>
How to Choose?
The standard of care is that patients with opioid use disorder should first be treated with naltrexone ER before opioid agonist treatment to prevent opioid dependence

a) True
b) False
Knowledge Check

- Naltrexone ER should be first line therapy for people with opioid use disorder who are incarcerated

- A) True
- B) False
Which Patients are Likely Better for Agonist Therapy?

- Longer history of use
- Patients with history of overdoses, particularly following detoxification
- Patients with serious mental illness, disorganized, homeless
- Patients who have been opioid-free but never felt “normal”
- Patients with chronic pain requiring chronic opioid treatment
Selecting Patients for Antagonist

- Patients not interested in, or able to be on, agonist maintenance
- Shorter history of use
- Those with high degree of motivation for abstinence
- In professions where treatment with agonist is controversial (healthcare professionals, pilots)
- Patients successful on agonist but who want to try abstinence
- Patients who are abstinent but at risk for relapse
“No One Size Fits All”

- Guidelines developed by ASAM 11/2015
  - physicians must use clinical judgment considering multiple issues
- Patient preference
- Severity of opioid use disorder
- Patient history of treatment response
- Co-existing medical and psychiatric conditions
- Other medications and potential for interactions
- Other substance use disorders
- Job, travel, transportation, family needs
- Pain
- Patient beliefs about specific medications, in collaboration and discussion with family
- *Pending incarceration
Summary
Summary

- Menu of options

- Agonist maintenance is preferred treatment and length should be for as long as the patient benefits

- Induction onto extended-release naltrexone can be an effective strategy for relapse prevention for those unable or not interested in agonist

- Methadone maintenance treatment consists of daily methadone
  - Requires opioid treatment program

- Antagonist treatment consists of once monthly injection
  - Anyone can prescribe naltrexone
Rebecca

Rebecca is a 28 yof OUD/IV heroin x 5 years, past buprenorphine program x 6 months, intermittent self non-prescribed buprenorphine management, requests resumption of treatment.

Requesting more than 16 mg daily and running short.

Considerations:

- Dose, engagement in care, comorbidity
- Home or office induction?
- Length of treatment/taper?
- Diversion
- Pseudo-addiction
Kevin

Kevin is a 52 year old software engineer with a remote hx of AUD, ADD, MDD, 5 year OUD with recent escalation to heroin. Does not want agonist therapy. Buprenorphine helps at 2 mg daily.

Considerations:

• Why doesn’t he want agonist?
• Transfer from agonist to antagonist possible
• Comorbidities, co-occurring SUD
Celeste

Celeste is a 35 year old woman with a 10 year history of IV heroin OUD, AUD, binge eating disorder, major depressive disorder, sexual trauma. Tried buprenorphine several times, max dose, intensified treatment, but cravings and heroin use persist, significant abscesses, protracted relapse, intermittent ETOH. Can’t seem to get back on Buprenorphine.

Considerations:
• Safety – Bup vs Methadone, Overdose risk
• AUD and OUD -> Naltrexone?
• Structure
• Eating Disorder
• Dual Diagnosis
Naloxone/Narcan

• Overdose reversal
• Pure antagonist at the mu receptor
• 2006 – MA OPEN network
• Expanded nationally
• First responders, family, friends public, patients, school nurses
• Should be co-prescribed to all with OUD and family/friends
• Most have witnessed and or reversed overdose
Narcan has a stronger affinity to the opioid receptors than opioids like heroin or Percocet, so it knocks the opioids off the receptors for a short time. This allows the person to breathe again and reverses the overdose.
Knowledge Check

• If a person continues to overdose after being reversed by intranasal naloxone, he is clearly not interested in stopping/hasn’t hit his rock bottom yet. He should be encouraged to return when he is ready.

a) True
b) False
Intranasal Naloxone

6/16/16

I had my first overdose after 20 years of IV drug use. I can describe my thought and feelings after being saved by Narcan in one word: ALONE. GrATEFULLY this medication/drug is saving lives. Thank God, god bless keep the faith.

6/17/16

Today is my birthday and I have received the best present ever... another chance at life. So grateful for my family, so grateful for my health, so grateful for this program, and a grateful heart will never reverse.

NICK
Medication is a Necessary Tool

“Access to medication – assisted treatment can mean [the] difference between life or death.”

Michael Botticelli, October 23, 2014
Director, White House Office of National Drug Control Policy
Thank you!

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Resources

• Physician Clinical Support System for Opioid Therapies (PCSS-O), for Medication Assisted Treatments (PCSS-MAT).  http://www.pcss-mat.org
• Medication-Assisted Treatment for Opioid Addiction: Facts for Family & Friends http://store.samhsa.gov/shin/content/SMA09-4443/SMA09-4443.pdf
• Medication Assisted Therapy Toolkit  http://www.niatx.net/PDF/NIATx-MAT-Toolkit.pdf