Learning from Patients In Recovery (PIR): What should the internist know about methadone maintenance?

Session WB08, SGIM Meeting, Thursday, April 29, 2010

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Session Learning Objectives:
By the end of this workshop participants will be able to:
1. Dispel popular myths and address stigma about methadone maintenance treatment
2. Identify and address complications of methadone maintenance treatment
3. Address comorbidities in the context of a patient receiving methadone maintenance

CASES

Please choose one member of your small group who will be responsible for briefly (1-2 minutes) reporting back to the larger group lessons learned from your case discussion.

Case 1: Complications of methadone maintenance treatment
Ms. A is a 41 year old female returning for primary care follow-up after being seen in the emergency department for anxiety. She notes that leading up to the emergency visit she had been more stressed out and began to feel short of breath and developed tingling in both of her arms. She did not have any chest pain but felt repeated “fluttering” sensations in her chest that lasted for less than one second.

At time of emergency room evaluation her ECG showed a fast heart rate with a QTc interval of 486 msec. Her blood tests (electrolytes and complete blood count) were normal. The emergency department diagnosed her with a panic attack and prescribed a sedative (alprazolam (Xanax) 0.25 mg three times daily as needed), and propranolol 20 mg twice daily. They also suggested that she stop methadone because of a prolonged QTc interval, which they told her “may be dangerous.”

Ms. A is distraught. Methadone has been very helpful in treating her heroin dependence but what the emergency doctor said scared her. She also worries that since starting methadone she has gained fifteen pounds and that the methadone may be causing this. She asks her primary care doctor what she should do.

Past Medical History:
1. Panic disorder
2. Opiate dependence in remission on methadone maintenance therapy: patient began injection heroin use in teens and was treated with methadone maintenance. She did well for 5 years and gradually tapered off of methadone.
She relapsed to heroin within a year and restarted methadone. After several years on methadone, she gradually tapered and remained abstinent for 10 years until relapsing on hydrocodone following a dental procedure. Since restarting methadone several months ago she has done very well and is able to receive three take home doses per week.

Allergies: Penicillin

Medications: as above. No antibiotic use or use of over the counter antihistamines.

Family history: No history of unexplained passing out. No sudden cardiac death, no long QT syndrome. Father has hypertension and diabetes mellitus.

Review of systems: Nothing else significant

Exam
Vitals: blood pressure 117/80, heart rate 54, respiratory rate 12 breaths per minute, oxygen saturation 97% on room air, Body mass Index (BMI) 28
General: No distress
Neck: No distended neck veins (JVD)
Heart: S1 and S2 no added sounds
Lungs: clear to auscultation bilaterally
Abdomen: soft, non tender, bowel sounds present
Extremities: symmetric pulses, no edema, no clubbing, no cyanosis

ECG in clinic: normal sinus rhythm with a rate 53, QTc 414 msec.

Discussion points:
Please consider the following involving all members of your small group and from the perspective of both the physician and the patient:

1. What are the benefits of methadone treatment versus abstinence based treatment (counseling only)?
2. Has she been on methadone too long? Does she need to discontinue methadone? What are the risks and benefits of continuing/discontinuing methadone? How would you counsel her?
3. Is the patient’s weight gain caused by methadone?
4. Is the patient’s prolonged QT interval caused by methadone? What is Ms. A’s risk of sudden cardiac death?
5. What are take homes?
6. What are other risks or complications of methadone maintenance not mentioned in the case?

Report back to large group:
In a 2 minute summary, report back to the larger group the key points of your discussion of the case.
Please choose a different member of your small group who will be responsible for briefly (1-2 minutes) reporting back to the larger group lessons learned from your case discussion.

Case 2: Comorbidities in methadone maintenance

29 year old male iron worker comes to a new primary care doctor to discuss his hepatitis C diagnosis and his chronic back pain.

His last visit to a medical doctor was 6 months ago. He had gone to his primary care doctor at the time to receive his test results for hepatitis C. His doctor informed him that his test was positive and asked him if he had been using injection drugs. The patient admitted that he had started injecting heroin about a year before when his chronic pain medication – long-acting morphine – started to run short each month and he could no longer afford to buy extra medication off the street. The doctor was frustrated and told the patient he could no longer prescribe pain medication to him. The patient became distraught, stopped working, and increased his heroin use.

Known medical problems:
- Hepatitis C infection
- Chronic back pain since age 23 after a fall at work – He had head trauma and a concussion with this fall. He was treated initially with short acting opioid pain pills for acute pain and then had been prescribed long-acting morphine for chronic pain from age 23 to 28.
- Alcohol dependence in remission – The patient had been a binge drinker from age 15-18, then a daily drinker from 19-21 with 1 withdrawal-induced seizure. After being hospitalized at 21 for alcohol withdrawal, he went to detox, then a 28-day program, then a halfway house. He was active in AA until age 24 with a sponsor and home group, until after he injured himself and was taking opioid pain medications regularly. In the past year, he reports drinking only 1 beer on New Year’s Eve.
- Nicotine dependence – 15 years of 10-20 cigs per day

Today, he comes in to re-establish primary care and start fresh with a new doctor. Two months ago he went into a methadone maintenance program because he could not afford to buy heroin daily without breaking the law and he did not want to go to jail. He wants to start working again. He has cut back on his heroin use from 3 times daily to once weekly. He is grateful to no longer have to chase heroin every day, though he is now worried about his health which he feels he has been ignoring. He is also struggling with sleep, anxiety, and low mood. People in the clinic have offered him benzodiazepines, clonidine, and other pills to help him with his symptoms and to boost the methadone, which can give a buzz.

He wants his primary care doctor to address his hepatitis C infection, his back pain, and his anxiety and depressive symptoms.
Discussion points:
Please consider the following involving all members of your small group and from the perspective of both the physician and the patient:

1. Hepatitis C infection is common in injection drug users and therefore in methadone maintenance patients. What can primary care doctors do to address hepatitis C infection?

2. What are the other addiction, mental health, and medical problems that are common in methadone maintenance patients?

3. How can primary care doctors better help patients with chronic pain that have developed opioid addiction? What role can methadone maintenance play in chronic pain and how can the doctor facilitate a referral to a pain specialist?

4. What about AA or other self-help groups? Could they help this patient now? Are they treatment?

5. What should the primary care doctor do about the anxiety and depressive symptoms in the setting of the patient being offered street prescription pills?

6. Should the primary care doctor coordinate his care with methadone providers? If so, how?

Report back to large group:
In a 2 minute summary, report back to the larger group the key points of your discussion of the case.

POSSIBLE DISCUSSION POINT RESPONSES

Please note: This covers some of the possible responses but not all the possible responses. Your small group hopefully touched on some of these points but also went beyond what is included.

Case 1: Complications of methadone maintenance treatment

Discussion points:

1. What are some of the factors to consider when comparing methadone treatment and abstinence based treatment (counseling only)?
   - Abstinence and methadone philosophies are not mutually exclusive
• Some individuals may require ongoing methadone indefinitely to help them remain illicit-drug free, some may begin with methadone and transition to a medication-free state, and others may not require methadone at all
• A combination of treatment modalities may be utilized over the course of treatment and recovery
• Treatment needs to be individualized, the right treatment is the treatment that works for that patient
• Detoxification alone is rarely effective

Methadone treatment can
• alleviate withdrawal symptoms
• blunt/ eliminate effects of additional opioid use
• provide a daily behavioral structure
• provide observed dosing with gradual increase in clinic privileges
• provide an opportunity for counseling treatment

Drawbacks can include: regulations and restrictions, stigma, inconvenience of daily clinic attendance, side effects

2. Has she been on methadone too long? Does she need to discontinue methadone? What are the risks and benefits of continuing/discontinuing methadone? How would you counsel her?

• Methadone treatment should be individualized and is patient-specific.
• Some patients are on methadone for months, others for years, and still others indefinitely
• The benefits of methadone treatment need to be weighed with the adverse effects and in the absence of adverse effects methadone maintenance can be continued as long as the patient and provider feel it is safe and beneficial
• Risks include possible QTc prolongation, sedation
• Benefits of methadone treatment impact the individual and the community and include: risk reduction, improved health, improved social functioning, decreased crime, and decreased cost to society
• Methadone if discontinued must be stopped gradually to prevent opiate withdrawal

3. Is the patient’s weight gain caused by methadone?
• Patients often report weight gain on methadone maintenance
• The cause for weight gain is likely multifactorial
• Some possible causes include:
  o Better eating habits when patient is not chasing drugs
  o Decreased physical activity when patient is not chasing drugs
  o Increased carbohydrate/sweets craving
4. Is patient’s prolonged QT interval caused by methadone? What is Ms. A’s risk of sudden cardiac death?
   - Other possible causes of QTc prolongation should be explored including: electrolyte disturbances (hypokalemia, hypomagnesemia), medications (antibiotics, antifungals, antipsychotics), other illicit substances (cocaine, amphetamines), etc.
   - personal medical history of long QT syndrome, cardiac conduction defects, arrhythmias, syncope episodes, seizures, palpitations, dizziness and lightheadedness, and a family history of long QT syndrome, cardiac conduction defects, arrhythmias, syncope episodes, seizures and sudden or unexpected death should be part of the medical assessment
   - Ms. A’s risk of cardiac death is extremely low. Her QTc is now normal. Estimate of maximum risk of sudden cardiac death in methadone patients is 0.06 cases per 100 patient years.

5. What are take homes?
   - Take homes are methadone doses that the patient takes on his or her own at home or in another unsupervised setting
   - Methadone maintenance is federally regulated and initially dispensed 6-7 days/week as directly-observed therapy at the clinic
   - A single take home dose can be given for a day that the clinic is closed for business, including Sundays and State and Federal holidays
   - Additionally take homes can be “earned” based on the following criteria:
     - Absence of recent abuse of drugs
     - Regularity of clinic attendance
     - Absence of behavioral problems or criminal activity
     - Stability of patient’s home environment and relationships
     - Length of time in treatment
     - Assurance that take home can be safely stored at patient’s home (use of a lock box)
     - If the rehabilitative benefit the patient derives from decreasing clinic attendance outweighs the potential risk of diversion
   - Different programs vary on the protocol for how and when take home medication is dispensed
   - Often after 3 months of meeting the above criterion patients can receive one take home dose per week

6. What are other risks or complications of methadone maintenance not mentioned in the case?
   - Opiate withdrawal if hospitalized or incarcerated
   - Interaction with other medications or drugs (esp., alcohol, sedatives)
   - Sleep disturbances
   - Sweating
   - Decreased libido/difficulty ejaculating
   - Urinary hesitancy
Case 2: Comorbidities in methadone maintenance

Discussion points:

1. Hepatitis C infection is common in injection drug users and therefore in methadone maintenance patients. What can primary care doctors do to address hepatitis C infection?
   - If needed, confirm hepatitis C status with HCV antibody testing
   - Obtain HCV RNA (viral load) testing
   - Vaccinate against hepatitis A and B
   - Provide prevention and risk reduction counseling and education
   - Counsel regarding avoidance of alcohol, Tylenol, and other potentially hepatotoxic substances
   - Provide treatment education and referral if indicated
   - If patient is undergoing treatment for HCV help treating provider monitor for side effects, drug interactions, toxicities, depression, and anxiety

2. What are the other addiction, mental health, and medical problems that are common in methadone maintenance patients?
   - Alcohol, benzodiazepine and cocaine induced mood/anxiety disorders are common
   - Substance-induced disorders usually resolve within 1-2 weeks after methadone initiation in most patients
   - Current Depression diagnosis in <10%
   - Personality disorders are the most common psychiatric diagnoses (33% males and 15% females have antisocial PD)
   - The rate of Post-Traumatic Stress Disorder (PTSD) among people with substance use disorders is 12 to 34 percent
   - Attention Deficit Hyperactivity Disorder (AD/HD) occurs in 5-25% of the adult substance abuse population

3. How could a primary care doctor better help a patient with chronic pain that has developed opioid addiction? What role can methadone maintenance play in chronic pain and how can the doctor facilitate a referral to a pain specialist?
   - Methadone can be helpful for chronic pain, BUT is less helpful when given in 1 daily dose
   - Methadone split dose is more effective, BUT patient must handle doses responsibly
   - Pain management is more effective in conjunction with patient’s physician
   - Methadone is NOT effective for acute pain when patient is tolerant to maintenance dose.
   - Must use higher and more frequent doses of short acting opioids in addition to methadone maintenance dose
   - Effective communication between health care providers is essential
4. What about AA or other self-help groups? Could they help this patient now? Are they treatment?
   - Many patients find AA and self-help groups helpful
   - These treatment modalities can be used alone or in conjunction with other treatment approaches
   - AA and self-help groups are often most effective used in conjunction with other treatment approaches
   - Each AA and self-help group has a different philosophy, composition, and “feel”; it is important to try several groups until one finds a group where they are comfortable
   - American Psychiatric Association and American Society of Addiction Medicine refer to AA and other self-help programs as important components of disease management but not by themselves as treatment

5. What should the primary care doctor do about the anxiety and depressive symptoms in the setting of the patient being offered street prescription pills?
   - Benzodiazepines are no longer the standard of care for chronic management of anxiety
   - Patients with addiction history may be at risk for misusing benzodiazepines
   - Methadone and benzodiazepines have synergistic sedating effects
   - Many antidepressants are effective in the management of both depression and anxiety
   - Behavioral counseling may be a useful adjuvant to these medications.

6. Should the primary care doctor coordinate his care with methadone providers? If so, how?
   - Effective communication and coordination of care improves addiction and medical treatment outcomes and reduces drug-drug interactions and adverse events
   - Obtaining a signed authorization of record release from the patient will allow a two-way exchange of information between the patient’s methadone provider and medical provider

RESOURCES

Articles

Finding Treatment
SAMHSA’s Treatment Facility Locator.
• Searchable directory of drug and alcohol treatment programs around the country that treat drug abuse, alcoholism, and alcohol abuse problems.
• Available at http://findtreatment.samhsa.gov/images/loc_short.pdf

NIDA’s National Drug Abuse Treatment Clinical Trials Network List of Associated Community Treatment Programs: http://www.drugabuse.gov/CTN/ctps.html

Office-Based Buprenorphine Certification http://buprenorphine.samhsa.gov/howto.html

Opioid addiction and methadone background info
1. Why do people use drugs?
   • To feel good
   • To feel better

2. Why is heroin so pleasurable?
   • Heroin is highly lipid soluble
   • Crosses blood brain barrier within 15 seconds="rush"
   • After IV administration 68% heroin in brain compared to <5% of morphine
   • Within 30 minutes metabolized to morphine
   • HEROIN is a prodrug of MORPHINE

3. Addiction is a Treatable Brain Disease

4. Prolonged substance use causes neurochemical and molecular changes in the brain, which alter:
   • Metabolic brain activity
   • Gene expression
   • Receptor availability
   • Sensitivity to environmental cues
5. Chronic Opioid Withdrawal
   - Lasts months to years
   - Secondary to derangement of endogenous opioid receptor system
   - Symptoms
     - generalized malaise, fatigue
     - poor tolerance to stress and pain
     - craving for opioids
     - restlessness, insomnia

6. Opioid Detoxification Outcomes
   - Low rate of retention in treatment
   - Low rate of achieving abstinence
   - Low rates of success in maintaining abstinence
     - < 50% at 6 months
     - < 20% at 12 months

7. Methadone Hydrochloride
   - Full opioid agonist available in tablets, oral solution, parenteral
   - PO onset of action 30-60 minutes
   - Duration of action
     - 24-36 hours to prevent opioid withdrawal
     - 6-8 hours analgesia

8. Goals of methadone treatment for opioid dependence
   - Relief of withdrawal symptoms
     - Low dose (30-40mg)
   - Opioid blockade
     - High dose (>60mg)
   - Reduce opioid craving
     - High dose (>60mg)
   - Restoration of reward pathway
     - Long term (>6 months)

9. Why Maintenance?
   *Because it Works…*
   - Death rate lowered by 70% for opiate users on Methadone
   - “A clear consequence of not treating...is a death rate more than 3 times greater…” NIH Consensus Statement JAMA 1998

10. Methadone Maintenance Treatment
    *Highly Structured*
    - Daily nursing assessment
    - Weekly individual and/or group counseling
    - Random supervised toxicology screens
    - Psychiatric services
Medical services
Methadone dosing - Observed daily ⇒ “Take homes”

11. Most useful question to determine treatment success…
   - How long should maintenance treatment last?
   - Methadone Maintenance Limitations
     - Highly regulated - Narcotic Addict Treatment Act 1974
     - Created methadone clinics (Opioid Treatment Programs)
     - Separate system not involving primary care or pharmacists
     - Limited access - 5 states: 0 clinics, 4 states: < 3 clinics
     - Inconvenient and highly punitive
     - Mixes stable and unstable patients
     - Lack of privacy
     - No ability to “graduate”
     - Stigma

12. Methadone and QT prolongation
   - Methadone may prolong the QT-interval resulting in torsade de pointes.
   - Its package insert now contains a black box warning.
     - www.fda.gov/cder/foi/label/2006/006134s028lbl.pdf
   - Predisposing risk factors: bradycardia, hypokalemia, hypomagnesemia, hypocalcemia, structural heart disease, and family history.

13. QTc interval screening in methadone treatment
   The panel recommended that clinicians treating patients with methadone should:
   - inform patients of arrhythmia risk;
   - ask about structural heart disease, arrhythmia, and syncope;
   - measure pretreatment QTc and conduct repeat measures at 30 days and annually while patients are receiving methadone or more often if the dose is >100 mg a day (or if they have unexplained syncope or seizures);
   - discuss the risks and benefits and increase monitoring if the QTc interval is >450 ms but <500 ms;
   - consider discontinuation, dose reduction, or elimination of concomitant arrhythmia risks (e.g., medications that cause hypokalemia) if the QTc interval exceeds 500 ms;
   - be aware of other medications that could prolong the QTc or slow elimination of methadone.
   - The panel also noted that the guideline may not apply to patients with terminal, intractable cancer pain.

14. What is the risk?
   - Among 200 Norwegian patients in an ECG sample,
     - 28.9% of those receiving methadone had some QTc prolongation (>450 ms), and 4.6% had QTc prolongation of >500 ms
     - A positive dose-dependent relationship was observed between methadone and QTc interval.
• The mean dose of methadone in the ECG sample was 111 mg per day.
• All patients with a QTc of >500 ms were on methadone doses of 120 mg per day or higher.

15. Among patients in the OAT/mortality comparison sample,
• During the first month of methadone, 1 death among 3850 methadone initiations was attributable to potential methadone-associated cardiac arrhythmia.
• In 6450 patient-years of observation, 4 deaths were identified in which QTc prolongation could not be excluded as the cause, for a maximum mortality rate of 0.06 per 100 patient-years

16. Methadone for pain
• Use of methadone for pain has increased dramatically in last 5-10 years
• Typically dosed TID
• Therapeutic window is narrow in opioid-naïve
• Cross-tolerance is incomplete in opioid-dependent
• Start low and go slow (2.5mg, increase once weekly by no more than 5-10mg daily dose)

17. **Physician Clinical Support System...**
• answers questions about opioids, including methadone, for treatment of chronic pain
• answers questions about use of buprenorphine for treatment of opioid dependence
• is free, for interested physicians and staff
• is supported by SAMHSA through the Center for Substance Abuse Treatment (CSAT) and administered by the American Society of Addiction Medicine (ASAM)
• [www.PCSSmentor.org](http://www.PCSSmentor.org)
• PCSSproject@asam.org