Swinging Pendulum
Where are we?

“Opiophobia”
Fears of addiction
Fears of regulation
REMS

Pain as 5th Vital Sign
“No addiction with pain treatment”
“Pain blunts euphoria”

Goals

• Provide overview of intersection of palliative care and addiction
• Review tools for screening for risk of opioid misuse
• Review strategies including interdisciplinary approach for the management of pain and opioid misuse in palliative care setting
Misuse of Prescribed Opioids

• Overdose deaths from non-medical use is a public health crisis
• Most non-medical users obtain from friend or family member
Response to Crisis

- Prescription Monitoring Programs
- Mass BORM licensing requirement for pain
- REMS programs for opioids
- Tamper-resistant products
- State-level regulations for non-tamper resistant formulations
- Insurance, pharmacy restrictions

Prevalence of Substance Abuse in Palliative Care

- 12-24% of an inpatient palliative care population had history of alcohol abuse
- 3% psychiatry consults at tertiary urban cancer center for issues related to substance use disorders

Survey of Hospices in VA

- 43% required mandatory substance abuse training
- 44% had policies regarding screening for substance abuse in patients
- Policies regarding screening for diversion in patients (21.7%), and families (17.4%) were rare.
- 38% hospices agreed that substance abuse and diversion was a problem for their agency, and these agencies were more likely to have written policies or mandatory training.

**Problem in Oncology**

- Pain is very prevalent in cancer
  - 64% with advanced/metastatic disease
  - 53% patients at all stages
  - 33% after curative treatment
- 40% survivors live longer than 10 years
- Little is known about the prevalence of addiction or opioid misuse in oncology patient

*van den Beuken-van Everdingen MH et al. Ann Oncol. 2007 18(9 1437-46)*
*Del Fabbro E. J Clin Oncol 2014; (32) 16: 1734-1738.*

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**Heterogeneity of Pain Experienced by Cancer Patients**

- Longer survival = more potential opioid exposure
- Multiple different types of pain possible
  - Acute or chronic, cancer- or treatment-related pain
  - Chemotherapy, radiation, and/or surgical
  - Acute or chronic non-malignant pain
- Duration of therapy similarly variable, may be:
  - During active treatment
  - Through survivorship with NED status
  - In end-of-life phase

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**Problem in Oncology**

- Retrospective review of 114 cancer patients in outpatient palliative care clinic
- 43% medium to high risk by ORT
- Young age, personal history of alcohol or illicit drug use were most common risk factors
- 40% with UDS obtained, 45% “abnormal” findings

*Barclay JS, Owens JE, Blackhall LJ. Supp Care Cancer 2014. 22(7); 1883-1888.*
Problem in Oncology

- Retrospective single center study - 49/114 patients referred to outpatient palliative care clinic were moderate or high risk (high risk 25%)
- Family history of alcohol use and history of depression were most common; similar to most common risk factors in non-cancer populations


Advanced Illness / End-of-Life: Why Care About Treating Substance Abuse?

- Improved adherence to oncologic/medical therapy
- Lessens chance of under-treatment of pain and symptoms → lesser motivation for aberrant behaviors
- Help avoid adverse interactions between illicit drugs and prescribed medications
- Enables greater attention to EoL human growth that overlap with “recovery” (making amends, taking responsibility)
- Help stabilize social support network otherwise weakened / alienated by ongoing abuse


Oncology patients have predisposing risk factors or pain amplifiers

- Alcohol and/or tobacco use, personal or family history
  - 17-33% rate of alcoholism in patients w/ advanced cancer referred to palliative care
- Depression
- Generalized anxiety disorder
- PTSD
- Chemical coping
- Childhood adversity / preadolescent sexual trauma
- Delirium
- Somaticization

Del Fabbro E. J Clin Oncol 2014; (32)16: 1734-1738
Defining Addiction

- Distinct from tolerance, physiological dependence
  - (both expected with opioids)
- Use despite harmful consequences, physical and psychosocial
- Term can be stigmatizing

Identifying Substance Abuse in Palliative Care

- Opioids and other controlled substances are commonly used and are effective for symptom control
- Tolerance, dependence expected with chronic use
- Potential for misuse must be weighed against potential for under-treatment of pain

Case

TH 18 year old male with widespread testicular cancer presenting with multiple sources of pain.

Treated with escalating doses of opioids to manage this despite fact that cancer was responding to treatment.
Spectrum of Patients

- Patients currently using illicit substances
- Patients with history of substance abuse, now abstinent
- Patients with history of opioid abuse now on opioid maintenance therapy
- Patients who develop opioid/substance misuse/abuse during care for a life-limiting illness

Opioid Misuse on a Continuum

Adherence  Abuse

Opioid Misuse

Addiction
Non-medical use
Aberrant Drug-Taking Behaviors
Low Risk
Aberrant Drug-Related Behaviors

- No single behavior defines substance abuse in a medically ill population
- Consider a spectrum of abnormal behaviors that raise awareness of potential problems with drug use
- Addiction is a binary concept

Behaviors less suggestive of addiction

Behaviors more suggestive of addiction

Aberrant Drug-Related Behaviors

- More suggestive of substance use disorder
  - Selling prescription drugs
  - Forging prescriptions
  - Stealing drugs from others
  - Injecting oral formulations
  - Obtaining prescriptions from non-medical sources
  - Concurrent use of alcohol or illicit drugs
  - Repeated dose escalation or noncompliance
  - Deterioration in functioning at work, with family or socially
  - Resistance to changes in therapy despite evidence of adverse effects

Aberrant Drug-Related Behaviors

- Less suggestive of substance use disorder
  - Aggressively complaining of the need for more drugs
  - Hoarding drugs
  - Requesting specific drugs, dosages, or routes
  - Openly acquiring drugs from other medical sources
  - Use of a drug to treat symptoms other than those it was prescribed for
  - Occasional dose escalation
  - Reporting unintended psychic effects
  - Expressing anxiety about recurrent symptoms
  - Resistance to change in therapy with tolerable adverse effects
Differential for aberrant behaviors

- Opioid use disorder
- Tolerance
- Acute Pain
- Opioid induced hyperalgesia
- Uncomfortable affective state
- Withdrawal
- Diversion

Chemical Coping

- Patients take medications to treat anxiety and depression
- Key Clinical Features:
  - Alexithymia (decreased ability to identify and describe emotions to self)
  - Somatization
  - Overly drug focused
  - Unmotivated to explore non-drug interventions
  - Little progress toward psychosocial goals
  - Medicate to point of sedation which is a welcome side effect
- Interventions:
  - Goal is to help patients distinguish “pain” from anxiety and to demonstrate that there is specific relief available for each
  - Provide structure
  - Must decentralize the opioids as a coping tool
  - Limit or omit PRN’s, focus on long-acting opioids

Case

- TH became increasingly focused on his opioid medication regimen as well as benzodiazepine given for nausea.
- Tensions developed at home, mother asked for him to see psychiatrist regarding his medication use.
Managing the Chemical Coper

• Whenever possible, simplify drug regimens (ie, prescribe longer-acting medications to reduce overall number of pills available to a patient at any one time).
• Decentralize opioid use in these patients (ie, always reinforce that opioids are part of the full regimen and not the sole focus).
• Encourage or require psychotherapy and other adjunctive modalities to be part of the treatment approach.
• Focus on teaching coping strategies as alternate choices to reaching for a pill bottle in times of stress or emotional upset.

How to Assess for ADRB

• Comprehensive history and physical
  • Physical symptoms
  • Psychiatric symptoms
  • Psychosocial assessment, coping
  • Spiritual history
• Non-judgmental approach
• Open-ended questions
• Gently probe if warning signs

Case

• TH admitted to snorting his opioids to “get high”
• Problematic drug use was interfering with his cancer treatment
Opioid Risk Assessment

- Two tools screen for risk of opioid misuse
- Validated in chronic non-malignant pain populations
  - ORT 5 item tool
  - SOAPP 14 item tool
- In a study of 48 chronic pain patients, SOAPP was more sensitive than ORT


ORT in Palliative Care

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Elements of Opioid Agreement

- Expectations of the Patient
- Explain the role of the prescriber
- List risks and benefits of the proposed therapy
- Designate a signal pharmacy
- Provide a rational for your policy

Urine Drug Testing

- Aim for patient-centered, non-punitive testing
- Widespread testing reduces stigma
- Forensic testing vs compliance testing

Urine Drug Testing – Know Your Tests

- Urine pH, creatinine can also be measured to confirm specimen
- GC/MS, HPLC, immunoassay methods
- Routine UDT – low sensitivity for synthetic, semi-synthetic opioids
  - Fentanyl
  - Methadone
  - Oxycodone
  - Meperidine
Case

- TH was admitted to inpatient substance abuse treatment and initiated on buprenorphine for opioid maintenance therapy
- He was able to complete treatment for his cancer including autologous stem cell transplant

What We Know…

Opioid Use Related Medical Issues

- Infectious disease
  - Most common route of transmission for new cases is IVDU
  - 60-80% Hep C and 30% HIV: 5 years of IVDU
  - 80% of IVDUs with HIV also have Hep C
  - Coinfection triples the risk of liver disease and associated death
- Endocarditis, bactremia, soft tissue infections, falls
- AMA discharges from medical hospitalization
  - Greater likelihood of readmission within 30 days (32 vs 12%)
  - Subsequent admission for same or related problem in one month (28 vs 8%)
  - Longer stays in hospital for any readmission (median 5 vs 0 days)
Drug users utilize hospitals at high rates

Hospitalized in 1997 (%) Inpatient days

n=58,349 drug users in NY Medicaid program (Laine et al 2001)

Drug users may cause disruptions in hospitals

Left AMA Disruptive behavior Admit to misusing drugs in hospital Dead by 40mo f/u

n=124 drug users in London Hospital (Marks et al 2013)

How do we manage opioid withdrawal?
Is this patient drug seeking? Is it ok to give opioids?
How to manage acute pain given he is on buprenorphine?
Can we discharge her on morphine?
Pain is a subjective experience

“An unpleasant sensory and emotional experience, associated with actual or threatened tissue damage, or described in terms of such”

—(International Association for the Study of Pain, 1994)

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**Contributing factors to need for more**

- Opioid use disorder
- Tolerance
- Acute Pain
- Opioid induced hyperalgesia
- Uncomfortable affective state
- Withdrawal
- Diversion

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**Words**

- What does the pain feel like? (Sharp, dull, aching, etc)

**Intensity**

- On a scale 0-10, how is your pain now, at it’s worst/best, and the level you can live with

**Location**

- Where does it hurt? Does it radiate anywhere?

**Duration**

- When did it start? Does it come and go during the day? Is it always there?

**Aggravating/Alleviating**

- What makes it better or worse?
- Discontinue opioids (for chronic pain)
- Optimize mental health tx, and non-opioids
- Substance abuse treatment
- Buprenorphine or methadone?

- More intensive monitoring
- Maximize non-opioid strategies
- Optimize mental health treatment
- May be able to stay on opioids

- Continue treatment
- Standard monitoring

Assessment for “drug seeking” or non-medical use of opioids in the hospital setting

- Prior history
- Collateral
  - ORT
  - SDAPP

Assessment
Tx agreement
Monitor 4As

Universal precautions
Risk stratification
Medications
Non-pharmacologic
Guilty until proven innocent

- Assume pain is not real
- Unnecessary dosing of opioids is harmful.
- Patients must prove pain is real to receive treatment
- Allow some “innocent” patients go untreated to ensure no one ever receives opioids inappropriately

Innocent until proven guilty

- Assume pain report is real
- Untreated acute pain is harmful
- Clinicians must prove pain is not real to withhold treatment
- Allow some “guilty” patients go, in order to ensure all patients in pain receive treatment

Objective

- Evidence of tampering with IV lines ("white powder sign")
- Evidence of hoarding or cheeking of pain medications
- Illicit drugs found in room
- Witnessed using drugs
- Overdosing

Behavior

- Appearing intoxicated (pinpoint pupils, nodding off)
- NO change in pain rating after dosing
- Incongruence between pain score and behavior
- Preoccupation with pain medications
- Leaving floor without permission or at odd hours
- Appearing intoxicated after returning, or after visitors leave
- Requesting specific route or medication
- Visitors who are intoxicated

High Risk

- Evidence present for non-medical use
- Consider discontinuing opioids
- Maximize non-opioid strategies
- Buprenorphine? Methadone?

Moderate Risk

- Risk factors present that make monitoring necessary
- However; no evidence of non-medical use
- Continue opioids
- Maximize non-opioid strategies

Low Risk

- Risk factors not present
- No evidence of non-medical use
- Continue to monitor
- Continue opioids
Pain management in addiction

**Maintenance opioids (i.e. methadone or buprenorphine) should provide adequate analgesia**

Even if it's for acute pain, giving opioids to patients in MAT is harmful because it will result in a relapse

**Myths**

Adding opioids on top of methadone or buprenorphine will lead to an overdose

Patients in MAT requesting pain medications are always drug seeking

*Alford, 2006*

Pain management

<table>
<thead>
<tr>
<th>Methadone</th>
<th>Buprenorphine/naloxone</th>
</tr>
</thead>
<tbody>
<tr>
<td>• TID dosing allows for better pain management</td>
<td></td>
</tr>
<tr>
<td>• Covers withdrawal, tolerance, cravings while allowing for management of acute pain exacerbations</td>
<td></td>
</tr>
<tr>
<td>• Use prn short acting opioids for pain management</td>
<td></td>
</tr>
<tr>
<td>• NMDA receptor antagonist</td>
<td></td>
</tr>
<tr>
<td>• TID dosing allows for better pain management</td>
<td></td>
</tr>
<tr>
<td>• Higher binding affinity and partial agonism may make it harder for pain management in acute exacerbations</td>
<td></td>
</tr>
<tr>
<td>• With long standing use, can trial short acting opioids for pain</td>
<td></td>
</tr>
</tbody>
</table>
Goals of Pain Management

**Analgesia**
• Improvement in pain

**Activities of Daily Living**
• Physical, psychological, and social functioning

**Adverse Events**

**Aberrant Drug Taking Behaviors**
• Assess for behaviors suggesting non medical use or diversion of medications

Plan ahead

**Mild**
- Physical therapy
- Hot/cold
- Topical NSAIDs

**Moderate**
- NSAIDs
- Gabapentin 300 mg tid, up titrated
- Lidocaine patches

**Severe**
- Increase dose of bup/nal temporarily or split dosing
- Increase dose of non opioid interventions
- Add on TCA

Options for treating pain

1. Methadone or Suboxone + short acting opioid

2. Increase dose of methadone or Suboxone

3. Convert Suboxone to methadone and increase dose

4. Discontinue OMT and treat pain with other opioids
Continue methadone

Make sure to confirm dose

Continue regular dose, or reduce if needed (concurrent use of sedatives, hepatic dysfunction, etc)

If not, no more than 20-40mg on day 1

May divide methadone dose

Provide additional short-acting opioids if indicated

At discharge provide “last dose letter”

Stop buprenorphine

• Start full agonists and/or methadone (no more than 20-40mg on day 1)

• Plan for later re-induction

Continue buprenorphine

• Use additional buprenorphine or full agonists

• Maximize non-opioids

• May divide buprenorphine dose

Treatment Agreement

• Patient agrees to:
  - Use opioids only if it can improve pain and function
  - Abstain from using illicit substances during hospitalization
  - Adhere to treatment/diagnostic recommendations
  - Give urine for toxicology testing if requested
  - Allow room/belongings to be searched if indicated
  - Adhere to policies about leaving floor or allowing visitors
  - Sign release of information to coordinate care with all providers and family members

• Prescriber agrees to:
  - Treat pain using all appropriate methods including opioids
  - Not cut off opioids without adequate taper if it needs to be stopped
  - Treat withdrawal
Pros

- Manage withdrawal
- Manage acute pain
- Limited drug-drug interactions
- Monitored inductions
- Capture "reachable" or "teachable" moment
- Raise awareness about MAT in medical settings
- Can be discharged with prescription

Cons

- Requires knowledgeable clinicians (X-waiver)
- Inductions not straightforward
- Pain still may be an issue
- Nursing staff may be uncomfortable
- Pharmacy issues
- Cannot use if admitted for treatment of opioid use disorder
- Difficult to arrange follow-up

Starting Buprenorphine in inpatient/ED setting

Discharge patients with narcan education and Suboxone prescriptions

Supporting Research

- Liebschutz, et al.
- 139 patients admitted medically assigned to either 5 day detoxification (67) or linkage group (72)
- Linkage patients were more likely to enter buprenorphine treatment than those in detoxification group (52, 72.2 vs 2, 11.9%)
- Linkage patients also more likely to report less illicit opioid use at 6 month follow up and longer treatment retention
Supporting research

- BWH: 47 patients with opioid dependence started on bup/nal during a hospital admission
- Following induction patients were either given a direct referral or up to 4 week script
- Of those directly referred to a specific program, 59.1% had scripts within the next two months
- Of those who were provided with a script, 39.1% had a script within the next two months
- Overall, 46.8% of patients received a prescription within 2 months

D’Onofrio, et al
Randomized trial of 329 patients with OUD

Initiation in ED setting

<table>
<thead>
<tr>
<th>D’Onofrio, et al</th>
<th>Screening and Referral to Tx.</th>
<th>Modified SBIRT with facilitated referral</th>
<th>Screening, brief intervention, bup/nal ED initiation, follow up with primary care for ten weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Engaged in addiction treatment on 30th day</td>
<td>37% (38 of 102)</td>
<td>40% (50 of 111)</td>
<td>39% (69 of 114)</td>
</tr>
<tr>
<td>Reduction in number of days of illicit opioid use per week</td>
<td>5.4 -&gt; 2.3 days</td>
<td>5.6 -&gt; 2.4 days</td>
<td>5.4 -&gt; 0.9 days</td>
</tr>
<tr>
<td>Use of inpt addiction tx services</td>
<td>37%</td>
<td>35%</td>
<td>31%</td>
</tr>
</tbody>
</table>

Opioid overdose education and naloxone prescribing

If nothing else, "a dead addict can't recover"
Risk factors for opioid overdose

- Mixing opioids with other CNS depressants
- At least one other substance is typically found in overdoses
- Low tolerance
- Recent release from controlled environment
- Incarceration
- Residential treatment
- Use of Vivitrol
- Fluctuations in purity
- Recent physical changes
- Change in dealer
- Physical health
- Lung, liver, cardiac, kidney dysfunction
- Dose
- Higher dose (>100 mg morphine equivalents)
- Previous overdoses
- Using alone or in isolation

Signs and symptoms of opioid overdose

- Classic toxidrome:
  - Apnea
  - Stupor
  - Miosis (pinpoint pupils)

MASSACHUSETTS

Rate of Unintentional/Undetermined Opioid-Related Deaths
Massachusetts Residents 2000-2015
Massachusetts

![Graph showing percent of opioid deaths with specific drugs present (2014-2016)]

1. This is most likely illicitly produced and sold, not prescription fentanyl.
2. Prescription opioids include: hydrocodone, hydromorphone, oxycodone, oxymorphone, and tramadol.

References
