The PA's Role in PAIN Management

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HAZELDEN
A part of the Hazelden Betty Ford Foundation

Andy Mendenhall, MD
-Diplomate- American Board of Addiction Medicine
-Diplomate- American Board of Family Medicine
-Diplomate- American Academy of Pain Management

Practice:
- General Addiction Medicine
- Complex Pain/Addiction
- Opioid Detoxification
- Integrative Pain Management: broad referral network

Hazelden Betty Ford Foundation
- Largest Non-profit Treatment agency in the U.S.
- 22 Residential and Outpatient Facilities in all corners of the country.
  - Graduate School of Education
  - Research Center
  - Addiction Medicine Fellowship Program
  - “Cornerstone” of 12-Step Recovery
  - Innovative medical practice integration
    - Relapse prevention medicines
    - Buprenorphine/naloxone (Suboxone)
    - Naltrexone, Depo-Naltrexone (Vivitrol)
1. Primary Care Physician Assistant
   - Do your best to be opioid avoidant in your practice.
   - Screen for Substance use disorders among your patients.
     - Alcohol
     - Other illicit substances
     - Remember nicotine dependency is a risk factor for opioid misuse
   - When managing patients with pain and longitudinal “therapeutic” opioid dependency:
     - Do the same
     - See yourself as a person who can empower change
     - Embrace and potentially demand more treatment options

2. Specialty/Surgical PA
   - Do your best to be opioid avoidant in your practice.
   - Screen for Substance use disorders among your patients.
   - Discuss Risk/Benefit with patients:
     - Reward/Euphoria/Dependency
   - When managing patients with pain and longitudinal “therapeutic” opioid dependency:
     - Do the same
     - See yourself as a person who can empower change
     - Embrace and potentially demand more treatment options
“Red flags” in Chronic Opioid Therapy

• 1. Undue focus on medications
  – Refusal of other modalities or non-opioid medications
• 2. Increasing reports of pain, decreasing function.
• 3. Prescription Drug Monitoring Reports
  – Multiple prescribers
• 4. Morphine equivalent >120mg/day
  – 9-fold increase in death doses above 120mg/day

What do patients really do?

• 1. Est. 35% of patients taking C.O.T. addicted (4)
• 2. 71% of claimants on C.O.T. > 3 months are not taking their medication as prescribed. (5)
• 3. Among “chronic pain population” with sample of 939,000 urine drug screens (8);
  - 38% medication was absent
  - 29% non-prescribed opioid medication
  - 27% medication levels higher than prescribed
  - 11% illicit drugs

So what do opioids really do?

• Opioids bind to several sub-sets of receptors in the Brain and Spinal Cord
  – Mu-Receptor → Primary analgesic pathway
  – Kappa-Receptor → Primary hyperalgesia/tolerance
  – Sigma-Receptor → Secondary analgesic pathway
  – Delta-Receptor → Accessory pathway

• Tolerance and hyperalgesia immediately begin with the first dose of opioid.
  – G-protein linked Ca/Mg channel hyper-polarization
  – Receptor down-regulation
The importance of understanding tolerance/dependence

Considering the Therapeutic Window

- Opioid "Comfort" Zone
- Serum Level

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<tr>
<th>Considerations</th>
<th>Analgesia vs. Withdrawal Avoidance</th>
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The "experience" of opioid analgesia

- Occurs as a potentially novel and unique experience for each patient with each exposure.
  - Opioid analgesic → Mid-brain dopamine release
  - The SAME Survival-Based Reward/Reinforcement pathway that leads to addictive drive/behavior.

The human midbrain is tasked with integrating the 'intensity' of the pain signal with the 'intensity' of the analgesic signal.

Mismatch = Euphoria or Inadequate Analgesia
CEREBRAL ACTIVATION AND OPIATE CRAVING


CEREBRAL ACTIVATION AND OPIATE CRAVING

What is (Opioid) Addiction?

- We now use the term:
- “Opioid Substance Use Disorder”
  - Mild, Moderate, Severe
  - Fundamentally, ADDICTION is the following:
  
  **Compulsive Use Despite Harm**
  
  Rooted in the concept of “Salience” → That which is ‘important’
  - Addiction → Related to self-medication, chemical coping, regulation of emotions
  - Physical Dependency → Drives tolerance and behavior that can look like Addiction and transforms into Addictive behavior.

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What is Opioid Dependence?

- Refers to the physiologic state of requiring the presence of opioids in order to maintain homeostasis of CNS dopamine levels.
- Withdrawal is the hallmark of “Opioid deficiency” in the setting of physiologic dependency:
  - Severe emotional distress, Depression/Anxiety
  - Autonomic Instability
    - Sweating, tremor, diarrhea, mydriasis, excessive tearing and rhinorrhea.
  - PAWS “Post-acute withdrawal” symptoms persist for months.

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What is Opioid Hyperalgesia?

- Phenomenon that is different from opioid tolerance.
- Evolution of CNS to yield increased sensitivity to historically non-noxious stimuli. (alldynia)
- Mechanism: NMDA receptor activation by opioids directly and indirectly via multiple membrane complexes.
  - May be antagonized by NMDA-R antagonists
    - Ketamine, dextromethorphan
    - Methadone has inherent NMDA-R antagonist properties
    - Buprenorphine is a potent Kappa receptor antagonist

- Take Home: Opioids making pain worse. More opioids are not the answer…
Opiate induced hyperkatifeia

- Neuroadaptation in brain reward systems which parallels opiate hyperalgesia and may indicate a transition to addiction vulnerability.
- Opiate misuse in the context of pain management produces a hypersensitivity to emotional distress.
  - Mood changes linked directly to opiate therapy in the setting of a pain diagnosis.
- Continuous engagement of opponent processes leads to destabilization of homeostasis.
  - Analgesia vs. ‘treatment of underlying emotional state’
  - Pre-existing emotional state vs. one induced by the reward experience


Opiate HYPERKATIFEIA

- OVER TIME……

The challenge(s) for the opioid dependent patient?

- 1. Cope with their legitimate pain experience.
- 2. Take medicine appropriately.
- 3. Not use other drugs or alcohol.
- 4. Cope with opioid side effects:
  - Tolerance, Hyperalgesia, Hyperkateria
  - Constipation, sleep-disturbance, loss/diversion risk
- 5. Get their refill always on-time.

• ALWAYS AVOID WITHDRAWAL
The challenge(s) for the opioid prescriber?

1. Primum non nocare.
2. Patient/Family Expectations
   - Secondary gain?
3. DEA/State Compliance
   - Documentation (The Four-A's)
   - Drug Screening, PDMP, Material risk consent forms
4. Practice demands ➔ “stuff” rolls downhill….
5. Making Difficult decisions and confronting patients about
   the need to make changes.
   - MOST IMPORTANTLY in the patient that doesn’t have ‘issues’
     with their opioids.

The challenge(s) for the opioid prescriber?

1. Do something, anything other than prescribe an opioid…..
   - Patient population in Oregon/Washington, ‘primed’
2. Traditional Physical Treatment modalities;
   - Acute vs. Chronic
   - Physical Medicine ➔ TENS, PT, Hydrotherapy, Massage
3. Mental Health modalities;
   - Counseling, group therapy, Mindfulness-Based Meditation
4. Complementary Medicine;
   - Acupuncture, Naturopathy, Homeopathy
If you decide you are going to Rx Opioids…

1. Must ASSESS your patient completely
   – Opioid Risk Tool: ORT
   – Substance Use/Abuse History
   – Urine Drug Screening
   – Past Medical History
     • Old Records
     • Prescription Drug Monitoring Report
     • Pharmacy
     • Imaging

2. Discuss the facts about opioids
   – Grade C (at best) → Unlikely to be of benefit after 30 days
   – Physical Dependency requiring difficult detoxification

If you decide you are going to Rx Opioids…

1. Addiction Risk

2. Risk of Overdose Death if/when diverted or misused.
   – Security of medication
   – Pill counts
   – Urine Drug Screening with Ethyl Glucoronide (ETG)

3. EXPECTATION of sobriety from Alcohol

4. Risk of Overdose Death if/when diverted or misused.
   – Security of medication
   – Pill counts
   – Urine Drug Screening with Ethyl Glucoronide (ETG)

5. EXPECTATION of sobriety from Alcohol

6. Discuss how/why you will discontinue opioids
   – Absence of evidence that they are helping functionality.
   – Aberrant behavior or evidence of a “shift in the relationship.”
   – Maximum MED of 120mg, define what that means
   – You will refer back to these discussions in the future.

Opioid Risk Tool

The Four A's

- **Analgesia**: does the patient have effective pain relief?
- **Adverse effects**: are they severe, limiting, or are they controlled?
- **Activity**: evidence of increased function with opioids? Meeting activity goals?
  - Document what can be done that is different/improved.
- **Aberrant Behavior**: screen/monitor

Not getting the right answer on 4As?

**TIME TO TAPER/STOP!**

Identification of Substance Use Disorders-In Pain Patients

1. SUDs may or may not be present.
   - Past history
   - Tobacco
2. Often the “leverage” used to change therapy.
   - Anecdotally, often used as an excuse to abandon patients.
3. Tools for identification;
   1. Prescription Drug Monitoring Reports
   2. Urine Drug Screening
   3. Pill counts
   4. Validated Scale- SOAPP-R

SOAPP-R

- [soapp_r_sample_watermark.pdf](soapp_r_sample_watermark.pdf)
Changing Course in Opioid Therapy

- Follow-up evaluation and considerations for intervention.
  - Has salience for opioids changed?
  - Is there behavioral aberrance?
  - Affective change in patient?
  - Hyperalgesia?
  - Functionality?
  - Exploration regarding the resistance to change.
    - Secondary gain?
    - Substance Use Disorder?
    - Withdrawal avoidance?

- 1. These medications change neurobiology profoundly.
- 2. Nearly all patients have been through a withdrawal experience at some point.
  - PTSD-like response for some patients
  - Programmed withdrawal avoidance
  - Resistance to change is default pathway
- 3. Introspective/perceptive impairment.

Clinical Empowerment Thoughts

- 1. Intervention in the face of aberrant behavior is easy.
  - Abnormal PDMP
  - Abnormal UDS
  - SOAPP R score >22
  - Diversion
  - Other

- “There is a problem and the plan is…”
  - Opioid therapy is no longer safe or reasonable
Clinical Empowerment Options

- 2. What can you do?
  - Terminate care?
  - Terminate opioid therapy?
    - Tapering +/- comfort medications
    - Discontinuation +/- comfort medications
    - Opioid rotate to buprenorphine therapy
      - Dependency vs. Pain indications
  - Referral to OTP (opioid treatment program)
    - Methadone
      - Buprenorphine (allowed to Rx in ED/IC setting if direct referral follow-up)

Therapeutic options for detoxification

- 1. Opioid rotation and tapering
  - Short acting to long acting opioids
    - 25% taper per 2-4 weeks
  - Comfort medications;
    - Clonidine 0.1mg q8-12 h for sweating and agitation
    - Methocarbamol 500mg 1-2 po q6h for muscle spasm
    - Vistaril 25mg q8h for anxiety
    - Levsin 0.125mg q12h prn for diarrhea
  - Expect:
    - Complaints of Fatigue, Depression, Agitation
    - Complaints of Physical Pain, Reduced Functionality

Therapeutic options for detoxification

- 2. Rotation and Detoxification using sublingual buprenorphine.
  - Ambulatory/Outpatient Standard of Care
    - Applies to all patients;
      - Substance use disorder
      - Therapeutically Dependent
  - Requires DATA 2000 Waiver Application
    - Origin was to expand treatment for Opioid Substance Use Disorders
    - "Opioid Dependence" under FDA Labelling, DSM-IV Terminology
    - Elements:
      - 8 hours of education
      - Good intentions to help patients
      - Recommended: Mentorship
Buprenorphine

- Indication: Treatment of Substance Use Disorders
  - Sublingual
    - Generic Buprenorphine
    - Generic Buprenorphine/Naloxone
    - Suboxone Buprenorphine/Naloxone
    - Zubsolv Buprenorphine/Naloxone
    - Naloxone is not absorbed sublingually or orally
  - Acceptable dosing range 2mg-32mg
    - General recommendation <24mg

- Indication: Moderately Severe Persistent Pain
  - Transdermal Patch
  - Indicated dosing 5mcg/hr-20mcg/hr (70mcg/hr in Europe)
    - 20% of patients get a rash from the patch.

Buprenorphine Pharmacology

- 1. Mu- agonist with partial activation
- 2. Kappa- antagonist
- 3. NMDA- antagonist
- 4. ORL-1 (nociceptin agonist)
  - Higher doses lead to reduced analgesia
    - progressive recruitment
- 5. Delta- agonist
  - Mu/Delta heterodimers modulate the partial activation

Buprenorphine pharmacology

British Journal of Anaesthesia, 2005:94 (6); 825–34

Courtesy of Dr. Schiesser, Bellevue, WA
Dear Dr. Heit:

This is in response to your correspondence dated October 14, 2003, in which you requested the Drug Enforcement Administration (DEA) to respond to the following questions:

1. Can a clinician prescribe off-label use of buprenorphine with or without naloxone (Suboxone®/Subutex®) for the treatment of pain? If a clinician uses buprenorphine (Suboxone®/Subutex®) for the treatment of pain, does the prescriber have to have a DEA registration or does he or she need the special waiver that is required to prescribe buprenorphine for addiction?

The buprenorphine products Suboxone® and Subutex® are the two Schedule III narcotic medications currently approved for the treatment of opioid dependence under the federal Drug Addiction Treatment Act of 2000 (DATA). The off-label use of the sublingual formulations of buprenorphine (Suboxone®/Subutex®) for the treatment of pain is not prohibited under DEA requirements. However, off-label use does pose a dilemma for pharmacists. Currently, there is no requirement under the DATA for a qualified practitioner to put the Unique Identification Number (UIN) on a prescription for Suboxone® or Subutex® for maintenance or detoxification treatment.

On June 24, 2003, the DEA published a Notice of Proposed Rulemaking (NPRM) that will require qualified practitioners to include the UIN on all prescriptions written for either Suboxone® or Subutex® for narcotic addiction treatment. This requirement will be the only way to determine whether a prescription for Suboxone® or Subutex® was written for maintenance or detoxification treatment or some other condition. Buprenex®, a Schedule III, injectable formulation of buprenorphine, is approved and marketed in the United States as an analgesic and is widely used in the treatment of pain.

If a physician prescribes, dispenses or administers buprenorphine (Suboxone®/Subutex®) for the treatment of pain or for any other reason, a DEA registration is required because both products are Schedule III controlled substances. The DATA waiver specifically authorizes qualified practitioners to treat narcotic dependent patients, using FDA approved Schedule III-V narcotic controlled substances for maintenance and detoxification. The DATA waives the requirement for obtaining a separate DEA registration as a narcotic treatment program for physicians using the approved drugs for maintenance and detoxification; however, it does not apply to physicians using Suboxone® or Subutex® for the treatment of pain. A physician using Suboxone® or Subutex® for the treatment of pain would be required to register with DEA as practitioner with Schedule III privileges.

The Narcotic Addict Treatment Act of 1974 and the DATA amend the Controlled Substances Act (CSA) to allow for the use of opioid drugs to treat addiction either through maintenance or detoxification under specific criteria. Schedule II opioids approved for addiction treatment are limited to methadone and LAAM, and may only be administered and dispensed, not prescribed, by DEA registered Narcotic Treatment Programs. Schedules III through V opioids specifically approved by the Food and Drug Administration for use in addiction treatment may be prescribed, administered and dispensed by certified practitioners who have obtained the appropriate waivers from the Center for Substance Abuse Treatment.

The above legal allowances were established to allow for the treatment of addiction with opioid controlled substances. These limitations and requirements in no way impact the ability of a practitioner to utilize opioids for the treatment of pain when acting in the usual course of medical practice. Consequently, when it is necessary to discontinue a patient's opioid therapy by tapering or weaning doses, there are no restrictions with respect to the drugs that may be used. This is not considered "detoxification" as it is applied to addiction treatment.

I hope this information is of assistance to you in your continued efforts to promote the effective and responsible treatment of pain. If I can be of further assistance, please do not hesitate to contact me.

Sincerely,

Patricia M. Good,
Chief Liaison and Policy Section - Office of Diversion Control
Drug Enforcement Administration
U.S. Department of Justice

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**Buprenorphine for Pain is Legal with standard DEA Certificate**


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**Buprenorphine for Pain**

Sublingual Buprenorphine Is Effective in the Treatment of Chronic Pain Syndrome: Malinoff et. al.


- Case series of 95 patients- chronic non-cancer pain, Long-term opioid therapy
- Assessed Pain, Mood, Functional Capacity
- 60% of patients had dramatic improvement in mood and function
- 86% of patients had significant improvement in mood and function
- 6% discontinued due to inadequate analgesia, nausea, headache
- Mean daily dose: 8mg, duration of treatment was 8.8 months
- Well tolerated, no AEs

The only published study of its kind.
Ambulatory Buprenorphine Induction

1. How to start a patient on Buprenorphine
   - Opioid abstinence for 18-24 hours
     - Longer for ER most ER opioids 36-72 hours
     - Methadone 7-10 days
   - Comfort medications overnight before induction
   - In-office Urine Drug Screening
   - In-office observation
     - Clinical Opioid Withdrawal Scale (COWS)
     - Provide small doses of sublingual buprenorphine COWS >12
     - Comfort Medication
   - Close clinical follow-up and referral to treatment

Questions?

Summary Thoughts before Cases

1. All patients who take opioids are therapeutically dependent.
   - Most will be withdrawal avoidant.
   - Large percentage are addicted to opioids or other drugs/ETOH.
   - Many will eventually define a need for medical detoxification.
     - MUST consider this therapeutic option in ALL patients.
2. If you start opioids → Be clear about WHY?
   - Acute vs. Chronic pain
   - Analgesic Burden vs. Risk of Reinforcement/euphoria
   - Recognize that for chronic pain the literature does not support this plan of action.
Summary Thoughts cont.

• 3. If you are prescribing opioids for chronic pain conditions:
  – ASSESS RISK
  – Four A’s
  – Monitoring
  – Consider that there is a responsibility to the patient ALWAYS, particularly if you find a problem.
  • Not the time to “fire” and abandon someone’s care.
  • 4. When tapering opioids:
  – Slow and progressive tapers with tight boundaries
  – Consider buprenorphine rotation for pain.

References

References


Mendenhall Case #1

37 y.o. Dentist

- Axial Lumbar pain x 18 months. Self-referred from another pain management specialist.
- Generalized anxiety
- Effexor 225mg/day, Fentanyl 100mcg/hr every 48hours.
- Dull, throbbing pain in his back. Difficulty managing his fentanyl patches.
37 y.o. Dentist

• What do you need to know?
• History
• Examination
• What is your plan?
12 years of progressive axial back pain with radicular symptoms of burning and numbness into his legs and feet.

Vietnam Veteran with probable PTSD.

Difficulty sleeping due to his pain symptoms.

Additional Case Series
### Who has a substance use disorder?

<table>
<thead>
<tr>
<th>Patient A</th>
<th>Patient B</th>
<th>Patient C</th>
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<tbody>
<tr>
<td>Disabled 58 y.o.</td>
<td>Divorced 37 y.o. 2 kids</td>
<td>College-bound 26 y.o. C4-T2 bilat laminectomies with Posterior fusion of all levels</td>
</tr>
<tr>
<td>Six spine surgeries Cervical + Lumbar Asperger’s syndrome</td>
<td>L-Spine w/ a/p Fusion 4 level C bilat foramenotomies</td>
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**Patient A**
- Disabled 58 y.o.
- Six Cervical and Lumbar spine surgeries
- Axial spine pain
- Cervical and Lumbar Regions with radiculopathy

4 years of opioid acceleration - 100mcg/h fentanyl q48h
- 15mg oxycodone 1-2 q4h

Insomnia, Flushing, sweating and mood changes.
“I don’t like how I feel, I Hurt and my memory is changing.”
“I want to try something different.”

**PDMP Report:** Compliant

**PMD:** Compliant

**Salience:** None

**Withdrawal:** Yes

**Diagnoses:**
- Cervical Spondylosis 722.10
- Lumbar Spondylosis 752.20
- Phys. Opioid Dependency

**Medication Package:**
- Buprenorphine 4mg sl bid
- Hydromorphone 4mg bid prn
- Lyrica 100mg bid
- Cymbalta 80mg qhs
- Tizanidine 4mg qhs prn Topical NSAID prn
Who has a substance use disorder?

Patient B
Divorced 37 y.o. 2 kids - Manages Retail Store
L-Spine w/a/p Fusion - (total of 3 surgeries)

Previous medication package:
Hydrocodone/APAP 10/325 qid
Cyclobenzaprine 10mg bid

Divorce → Loss of insurance → meds stopped
"I'm sick and by back hurts, I can't stand on my feet all day to go to work" - No insurance

Who has a substance use disorder?

Patient B
POMP Report: Compliant
PMD: Compliant
Salience: None
Withdrawal: Yes
Diagnoses: Lumbar Spondylosis 752.20
Phy. Opioid Dependency 725.20

Initial Treatment Plan: buprenorphine 1 mg s.l bid
Cyclobenzaprine 10mg bid

New Insurance → Butrans 20 mcg/h, Lyrica 100 mg bid, Tizanidine 4 mg
Arms/Hands go numb → Severe multi-level Cervical DDD/Reduction → 4 level C Lam
Post-op → Rotate to pre-op regimen → Insurance change → s.l. Bupe+CBP
Key Outcome is FUNCTIONALITY

Who has a substance use disorder?

Patient C
College-bound 26 y.o.
C4-T2 bilat laminectomies with
Posterior fusion of all levels

Why?
Presented with fever and progressive dyspnea………

6th month of IVDA → C4 Epidural Abscess
4 week hospitalization → 6 week SNF → 10 months of rehabilitation
Spastic quadriplegia – ambulatory, loss of all fine motor
- neurogenic bladder, and L. ext. spasticity
Who has a substance use disorder?

Patient C

PDMP Report: Didn’t have one  
PMD: Didn’t have one  
Salience: Yes  
Withdrawal: Yes  
Diagnoses: Substance use disorder  
- Severe  
- Opioid w physiological dep.  
Quadriplegia

Reports persistent craving for opioids with extremity pain/spasticity  
ZERO pain - at his operative site

Referred on Suboxone 24mg, Diazepam 10x3, Baclofen, Vistaril,  
Month 29 - Suboxone 1mg/day, Clonazepam 0.5mg qhs, escitalopram 20  
Baclofen 10mg tid

Considerations - Discontinue benzodiazepine, rotate to Butrans patch

Thank You!

Andy Mendenhall M.D.  
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