The Interface of Pain Management and Chemical Dependency

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### ASAM Disclosure of Relevant Financial Relationships


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<th>Commercial Interests</th>
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Glossary of Terms

**Commercial Interest** - The ACCME defines a “commercial interest” as any proprietary entity producing health care goods or services, with the exemption of non-profit or government organizations and non-health care related companies.

**Financial relationships** - Financial relationships are those relationships in which the individual benefits by receiving a salary, royalty, intellectual property rights, consulting fee, honoraria, ownership interest (e.g., stocks, stock options or other ownership interest, excluding diversified mutual funds), or other financial benefit. Financial benefits are usually associated with roles such as employment, management position, independent contractor (including contracted research), consulting, speaking and teaching, membership on advisory committees or review panels, board membership, and other activities from which remuneration is received, or expected. ACCME considers relationships of the person involved in the CME activity to include financial relationships of a spouse or partner.

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**Conflict of Interest** - Circumstances create a conflict of interest when an individual has an opportunity to affect CME content about products or services of a commercial interest with which he/she has a financial relationship.
DEFINITIONS

- Use
- High risk use
- “Abuse” - Substance Use disorder (mild-mod)
- “Dependency” - Substance Use disorder (severe)
- Physical Dependency DOES NOT EQUAL a Substance Use Disorder
  - Severe Substance Use Disorder may exist without dependency
  - Dependency may exist (and even be at a high level) WITHOUT a Substance Use Disorder
Half of population uses alcohol on regular basis

Marijuana - 60 million

Cocaine/stimulants - 50 million

Opiates - 500-800k heroin, 2-4 million illicit use of licit opiates, ? 3-5 million in trouble with licitly prescribed opioids

Other - benzodiazepines, inhalants, MDMA & other psychedelics etc - ????
AT-RISK USE

- 25 million alcohol
- 15 million cocaine/stimulants
- 4 million marijuana
- 5-7 million opioids - ? number in pain management programs
- 2-3 million benzodiazepines
- ?? Numbers other drugs
12-15 million alcohol (M:F=3:1)
3 million cocaine/stimulants (M:F= 2:1)
3-5 million opioids (M:F = 3:1 for heroin but 1.5:1 in pain treatment)
1 - 1.5 million benzos/barbs etc. M:F = 1:3 (different in opiate treatment)
PAIN & ADDICTION-SEPARATE OR OVERLAPPING UNIVERSES??

- Old evidence: <1% of pain pt’s develop addiction problems (Boston collaborative pain study)
- New evidence: 30-50% of people with addiction have pain issues
- 10-15% of patients in pain treatment are dismissed for inappropriate drug-related behaviors
OBSTACLES TO TREATMENT

- Addiction programs will rarely, if ever, address pain issues
- Pain programs will rarely, if ever, address addiction issues (dismissal)
- Multidisciplinary programs for those with both problems virtually unknown
- Uncovering addiction should not automatically/necessarily mean dismissal from treatment
POSSIBLE SOLUTIONS

- Can we define high risk patient?
  - Current substance abuse
  - Prior history of opiate abuse
  - Prior history of other substance abuse
  - Personality disorders
  - Young male patients who smoke cigarettes
  - Demographic profiling??
    - Ethical, moral concerns
    - Legal concerns
    - Clinical concerns
POSSIBLE STEPS

- For those with pain and at-risk use/misuse, mild-mod SUDs
  - Continue pain treatment
  - Increased follow-up
  - Involve appropriate professionals
  - In-house treatment, particularly with addiction psychopharmacology agents when appropriate
POSSIBLE STEPS

- For patients with mod-severe substance use disorders
  - Referral to treatment programs
  - Prior arrangement to assure that program can appropriately manage clinical issues
  - Special concern for elderly or debilitated patients
PATIENTS WITHOUT PRIOR ADDICTION

- Opioids excellent drugs for reducing depression/anxiety, esp in those with trauma history (with AND without PTSD features)- trauma may be repressed!!
- Pt’s feel better secondary to psychoactive effects
- Tolerance develops much more quickly
- Dose escalation
- Pt does not recognize that they are treating underlying psychiatric issues rather than pain
- These may be majority of “new” abusers
Controlled Substance Agreements -1

- Consider standard policy of no opioid treatment on first visit
- Treatment contract with prior CD should include conditions for evaluation, UDS’s
- With current CD, immediate evaluation appropriate
- UDS for fentanyl, methadone, meperidine etc. before treatment
Controlled Substance Agreements - 2

- CSA’s should have clear language regarding expectations of BOTH patient and prescriber, and consequences of non-adherence
- Risks of physical dependency, including tolerance and withdrawal should be clearly stated; risks of substance use disorder (abuse/addiction) should be emphasized prior to treatment
- Advice should be given and documented that proper storage (lock box/safe, locked drawer/closet) essential, particularly if there at risk individuals in household (DO NOT KEEP THESE MEDICATIONS IN MEDICINE CABINET!!!)
- Proper disposal of unused medication should also be addressed, and laws may vary by State/locality - in general, do not flush down toilet, crushing pills/tablets and adding to kitty litter or other refuse; some localities have police or pharmacy “bring-back” days
Controlled Substance Agreements - 3

- CSA should include requirement for consultation with psychiatry, social work, addiction medicine/psychiatry, PT etc
- Adequate flexibility to keep you from boxing yourself into corners, with adequate rigor to keep patient from backing YOU into a corner (varies per practice) - some bright lines essential
- Fire the treatment, NOT the patient in most cases (except violence, threats, dealing etc.)
Alcohol - disulfiram, naltrexone, naltrexone ER (Vivitrol®), acamprosate

Opioids - naltrexone, nalmefine methadone, buprenorphine, Vivitrol®

Stimulants - many of ??? efficacy

Benzodiazepines - use of anti-epileptic drugs (AED’s)
DISULFIRAM (ANTABUSE)

- Old agent - 1940’s
- Blocks acetaldehyde dehydrogenase
- Build up of acetaldehyde -
  - Flushing, hypotension, headache, nausea, vomiting, hypotension
  - May cause syncope and vascular insufficiency, including MI and CVA
  - Rare (but potentially lethal) massive hepatic necrosis
DISULFIRAM

- Must be free from alcohol for 24 hours
- May last 7-10 days
- Deterrent drug, no direct effects on craving
- Requires education on diet, medications, colognes etc. (ESP. skin sanitizers near face)
- Other drugs act like disulfiram
  - Chlorpropamid
  - Metronidazole
NALTREXONE (REVIA®)

- Contraindicated with opioids
- Will precipitate withdrawal in those dependent on opioids
- Will block opioid effects in opioid naïve patients
- Does reduce craving and (esp.) alcohol reinforcement
  - Reduces heavier drinking
  - Best results are in combination with CBT
NALTREXONE

- May have use in those with EtOh/opioid abuse history being treated with non-opioids
- Available in injectable monthly (q28d) form - Vivitrol®, and non-approved implants (can last up to one year)
- Nausea, dizziness, headache common side effects
- Monitor LFT’s
- STRONGLY consider IR antagonist challenge before use, UDS, patient education!!!
NALTREXONE

■ When used for opioid abuse
  ■ Use of opioids in high doses to overcome block, esp. fentanyl, sufentanil
  ■ When patient stops naltrexone, hypersensitivity to opioids will temporarily occur- risk of overdose
  ■ If naltrexone induced w/d occurs use clonidine, sedatives, prn’s, ? fentanyl or sufentanil with anesthesia support
ACAMPROSATE (CAMPRAL)

- NMDA receptor modulator
- Reduces CNS glutamate
- Decreases craving, increases time of sobriety - works to promote abstinence rather than decreasing heavy use
- Few side effects
  - Mild GI symptoms (N/V, diarrhea, cramps)
  - Depression
  - Insomnia
FUTURE POSSIBILITIES

- Topiramate for alcohol abuse
- Topiramate studies have shown reduced alcohol craving, reduced use, improved quality of life
- Combinations of existing agents being studied
- Rimonabant (Acomplia®) and other CB1 receptor antagonists
OPIOID TREATMENT

- METHADONE PROGRAMS (MMTP)
  - Once daily rarely effective for pain
  - Use of multiple long-acting opioids may be problematic for program and patient
  - Patients without addiction history may not be appropriate for MMTP
  - Important to distinguish between PHYSICAL DEPENDENCY and addiction
BUPRENORPHINE

- Available since 2003 with the Drug Addiction Treatment Act of 2000
- **Suboxone®** - buprenorphine/naloxone
  - Filmtabs with buprenorphine 2 mg/naloxone 0.5 mg
  - Filmtabs with buprenorphine 8 mg/naloxone 2 mg
  - Filmtabs with buprenorphine 12 mg/naloxone 3 mg
- **Subutex®** - buprenorphine alone (2 & 8 mg film)
- Generics still available in 8 mg and 2 mg tablets, with/without naloxone
- **Bunavail®** - brand new formulation
  - Buccal film
    - Buprenorphine 2.1 mg/naloxone 0.3 mg
    - Buprenorphine 4.2 mg/naloxone 0.7 mg
    - Buprenorphine 6.3/naloxone 1 mg
- **Zubsolv®** - new formulation
  - Buprenorphine 1.4 mg/naloxone 0.36
  - Buprenorphine 5.7 mg/naloxone 1.4 mg
BUPRENORPHINE

- Partial mu agonist, kappa antagonist
- Will precipitate withdrawal in opioid dependent patients
- Effective against mild-mod. Pain, requires bid-qid dosing for pain management
- May be effectively used once daily in some patients
BUPRENORPHINE

- May be good choice in naïve pt’s with prior opioid history
- Ceiling effect - 24-32 mg, little dose escalation seen
- Use in pain treatment is off label!! (except for Buprenex® and BuTrans®)
- Toxicity low - partial agonist activity results in very low risk of respiratory depression
CLINICAL UTILITY

- ADDICTION
  - Physicians may obtain waiver to treat up to 100 patients with opioid abuse/dependency
  - Counseling, UDS’s need to be “available”
  - Pa-C’s, NP’s cannot prescribe
  - Urine screens for buprenorphine available
  - Suboxone may give + opiate test
    (? Secondary to naloxone positivity)
CLINICAL UTILITY

Pain
- 12-32 mg in divided doses (most <24) equivalent to methadone 40-80 mg
- Will block other opioids used to treat breakthrough pain (fentanyl or sufentanil may be first choice)
- Can be used without waiver per DEA/FDA response (possible insurance/pharmacy issues)
- **Off-label use!!!**
Protection against Overdose

- Naloxone (Narcan®) kits are available in intramuscular autoinjectors - Evzio®
- Naloxone kits, with syringes and 2 mg vials are available
- Naloxone intranasal kits have been available by pharmacists (CVS, Walgreens and others) who have produced them (not approved by FDA)
- Intranasal Naloxone (Mountainside Medical Products) are FDA approved and are available online
- Costs run from $30-100/kit, insurance coverage is variable, covered by most State Medicaid plans
- Educational presentations available for both patients and significant others/family members/clinic staffs
- Being recommended in ALL opioid treatment programs AND for pain management patients on opioids as well
- Check with your own State for regulations, availability, trainings
STIMULANTS

- No agent proven to be of benefit in RCT’s
- Antidepressants, esp TCA’s - not useful
- Other stimulants - mixed results
- AED’s - topirimate, carbamazepine, oxcarbazepine
- Novel agents - modafanil (and analogs)
- Several studies of GHB, N-acetylcysteine and baclofen have been promising
- Cocaine vaccine in trials
- Dopaminergic agents
  - Amantadine, bromocriptine - limited value
BENZODIAZEPINES

- Detoxification should be very cautiously approached esp. with barbiturate combinations
- High dose use may warrant inpatient treatment
- Use of AED’s in conjunction with short-term benzodiazepine tapers has been successful
Medical Marijuana Issues

- Many programs exclude patients on medical marijuana
- Many programs will dismiss patients who admit to, or are positive for marijuana use
- DVA now requires its Pain and Addiction programs to individualize evaluation and management of these patients!
- Little data to guide us!
- Levels may be helpful in differentiating those using for medical purposes and those using for euphoria
Management of Pain in Patients on Antagonist Therapy

- Patients on oral and ER Naltrexone (Vivitrol®) and on buprenorphine
- Usual opioids have lower association constants than do antagonists or partial agonists
- Use of regional anesthesia and non-opioid therapies should be maximized
- Use of high potency opioids preferred
  - Hydromorphone
  - Fentanyl
  - Sufentanil
Pseudo-addiction?

- Widely cited, but difficult to establish and prove/disprove
- Requires information from collaterals in patients' homes, workplaces
- Often best diagnosed in retrospect, when patients on appropriate doses of medication and aberrant behaviors stop
- More common in patients treated by PCPs than by Pain Management specialists
FUTURE DIRECTIONS

- Methods to detect higher-risk individuals - questionnaires, blood tests, genetic markers
- Focus on patients with trauma histories
- Rimonabant (and others)- CB1 receptor antagonists which may be the ‘gorillamycin’ of addiction
- Not treating pain patients like addicts!
MY FAVORITE DIRECTION

- NOT TREATING ADDICTS LIKE ADDICTS!!
Addicts are Patients

- Non-judgmental, empathetic therapy
- Treatment as another kind of pain patient
- Working in coordinated way with addiction treatment professionals
- Consider having addiction professionals as team members
- Consider having relationship with treatment program or even having “attached” buprenorphine treatment program
  - GI Clinics (hepatitis C patients)
  - Infectious Disease Programs (HIV patients)
  - “High Risk” Pain Programs within DVA hospitals
CONCLUSIONS

- High risk pt’s should be identified and appropriate treatment plan made
- Special care with patients with trauma history; watch for rapid escalation of dose & consider psychiatric evaluation for appropriate treatment
- Consider addiction psychopharmacology treatment, as well as psychosocial treatment in CD patients
- Pain programs should consider having addiction specialists as team members
- Pain programs should consider either strong connections with buprenorphine providers or have their own
- Remember -- we live in a world where pain/addiction co-exist, and where addiction may develop as consequence of pain treatment in those with NO prior history
Treat Addiction
Save Lives
Thank you!

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