The role of MOUDs in Managing comorbid OUD & Chronic Pain

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Disclosures

- I have the following relationships to disclose:
  - None
Substance Use Disorder ↔ Chronic Non-Cancer Pain

- CNCP is common among those treated for SUD
- SUD is common among those treated for CNCP
- Among lifetime SUD, lifetime CP prevalence >50%
  - Those in tx for SUD, CP prevalence as high as 75%
- Overall prevalence of current SUD among CNCP 3-48%
  - Lifetime prevalence of any SUD if have CNCP 16-74%
SUD ↔ CNCP

• Substance use as coping response to pain-related symptoms

• Substance use related injury leading to chronic pain conditions

• Diathesis-stress model
  • “Semi-dormant characteristics of the individual before the onset of chronic pain that are then activated and exacerbated by the stress of this chronic condition, eventually resulting in diagnosable psychopathology.”
SUD ↔ CNCP

• In 200 patients with CLBP, SUD preceded the onset of chronic pain
• In 421 patients with CLBP, no correlation between premorbid psychopathology and chronic pain disability
• In patients CLBP and SUD, SUD preceded LBP in 77% of patients with current and 63% with lifetime substance use disorders

Medications for OUD

- FDA approved MOUDs
  - Methadone
  - Buprenorphine
  - Naltrexone

https://www.samhsa.gov/medication-assisted-treatment/treatment#medications-used-in-mat
OUD: Methadone (PO)

- Doses of from 80-100mg/day have significant advantages, compared to lower doses, in reducing illicit opioid use and in retaining patients in treatment

- For most patients, a stable dose ranges from 80-120mg/day
OUD: Buprenorphine (SL, buccal, SQ, SD)

- Final stabilization doses of buprenorphine range from 2-32mg/day
- Average dose, 16mg/day
  - 24mg/day, most common maximum dose
- New implantable and injectable formulations
OUD: Naltrexone (PO, IM)

• Common dose is 50mg/day
Managing CNCP in patients with OUD

- Multi-disciplinary care teams
- Stepped care models
- Therapies
  - Non-pharmacologic tx
  - Non-opioid pharmacologic tx
  - MOUDs

Managing CNCP & SUD
## CNCP & OUD: Non-opioid Analgesics

<table>
<thead>
<tr>
<th>Medication</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>Potentiates analgesia</td>
</tr>
<tr>
<td>NSAIDS</td>
<td>Relieve numerous types of pain, especially bone, dental, and inflammatory, and enhance opioid analgesia</td>
</tr>
<tr>
<td>SNRIs</td>
<td>Relieve migraine, fibromyalgia, low back pain</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Efficacy in migraine prophylaxis, fibromyalgia, many neuropathic pains, vulvodynia, and functional bowel disorders</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Some efficacy for fibromyalgia, migraine prophylaxis, and neuropathic pain</td>
</tr>
<tr>
<td>Topical analgesics</td>
<td>Work locally</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>To abort migraine/cluster headache only</td>
</tr>
<tr>
<td>Muscle relaxants</td>
<td>Not recommended (acute period?)</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Cannabinoids</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>
CNCP & OUD: MOUDs

• *Very little data available*
• Higher doses may be required
• Shorter dosing intervals
  • Methadone (PO): BID-TID-QID dosing
  • Buprenorphine (buccal, SL): TID dosing
• Naltrexone: Not used, lacks analgesia
• Other opioids: Should be used with extreme caution
MOUDs: Efficacy for CNCP & OUD

• Buprenorphine meta-analysis
  • Beneficial effect on pain intensity overall
  • Small mean effect size in patients with comorbid chronic pain and OUD
  • Moderate-to-large effect size in chronic pain patients without OUD

• Buprenorphine vs methadone therapy
  • Both appear to improve chronic pain

Other Pharmacologic Agents?

• Ibogaine – psychoactive indole alkaloid investigated as potential agent to treat opioid addiction
  • Lacks data
  • Concerns about serious side effects

Thank You
<table>
<thead>
<tr>
<th>Parameter (characteristic)</th>
<th>Buprenorphine</th>
<th>Methadone</th>
<th>Naltrexone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacologic action</td>
<td>Partial agonist at the μ-opioid receptors and an antagonist at κ-opioid receptors</td>
<td>Full opioid agonist</td>
<td>Full opioid antagonist</td>
</tr>
<tr>
<td>FDA-approved clinical indication</td>
<td>Opioid-use disorder, pain</td>
<td>Opioid-use disorder, pain</td>
<td>Opioid-use disorder, alcohol-use disorder</td>
</tr>
<tr>
<td>Route of administration</td>
<td>Buccal film, subcutaneous extended-release injection, subdermal implant, transdermal patch</td>
<td>Oral, parenteral</td>
<td>Oral, intramuscular</td>
</tr>
<tr>
<td>Therapeutic dose</td>
<td>Orally: 8 to 16 (max 24) mg subcutaneously monthly; 100 mg to 300 mg subdermal implant; 71.2 mg every 6 months; transdermal patch; maximum 20 mg; replace every 7 days</td>
<td>80 mg to 120 mg daily</td>
<td>Orally: 50 mg daily or 100 mg orally every other day or 150 mg orally every third day</td>
</tr>
<tr>
<td>Frequency of administration</td>
<td>Orally: daily, every other day, 3 times a week; subcutaneously: monthly; patch: weekly; implant: every 6 months</td>
<td>Daily</td>
<td>Orally: daily, every other day or every third day; intramuscular: monthly</td>
</tr>
<tr>
<td>Protein binding</td>
<td>90%</td>
<td>85% to 90%</td>
<td>21%</td>
</tr>
<tr>
<td>Bioavailability</td>
<td>Buccal film: 48% to 65%; transdermal: 14%</td>
<td>Oral: 10% to 100%</td>
<td>5% to 60%</td>
</tr>
<tr>
<td>Half-life elimination</td>
<td>Buccal film: subdermal implant: transdermal patch: 24 to 48 hours; subcutaneous extended-release injection: 43 to 60 days</td>
<td>8 to 59 hours</td>
<td>4 to 13 hours</td>
</tr>
<tr>
<td>Onset of action</td>
<td>10 to 30 min</td>
<td>30 to 60 min</td>
<td>Up to 3 days; following 100-mg oral doses for 3 days (48% on day 1, 87% on day 2, 44% on day 3)</td>
</tr>
<tr>
<td>Duration of action</td>
<td>6 hours</td>
<td>5 to 8 hours</td>
<td>50 mg: 24 hours; 100 mg: 48 hours; 150 mg: 72 hours; intramuscular 4 weeks</td>
</tr>
</tbody>
</table>

Adapted from Medications for Opioid Use Disorder Treatment Improvement Protocol (TIP) Series KX 108.
Principles of chronic opioid maintenance for pain

- First try aggressive rehabilitative approach that may utilize opioids, but aims to restore function and reduce reliance on medications.
- Consider longer term treatment a serious undertaking that will require the commitment of both physician and patient.
- Ensure that other treatment options have been maximized.
- Consider opioid therapy as an adjunct; sole opioid therapy is rarely successful.
- Use goal directed therapy; set limits and goals and agree these.
- Use of a written agreement, contract or consent is helpful for setting out terms of treatment, terms for discontinuing treatment, and a clear statement of likely benefits and risks.
- Unless pain is occasional, base regime on long-acting opioids, and avoid breakthrough medication.
- Ensure careful and regular follow-up.
- Monitoring of opioid use is helpful using pharmacy databases, pill-counting or urine toxicology.
- Be prepared to wean and discontinue if treatment goals are not met.
- Maintain good documentation.