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Intermountain Project ECHO
Pain Management
Buprenorphine for Chronic Pain
May 3rd, 2022

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Intermountain Layton Family Medicine and Chronic Pain
Disclosure

The content of this presentation does not relate to any product of a commercial entity; therefore, we have no relationships to report.

Off-label indications will be discussed.
At the conclusion of this activity, participants should be able to successfully:

• Analyze the pharmacology and use of buprenorphine in the setting of chronic pain management
• Compare the dosing relationship between buprenorphine and opioid agonists
• Develop a simple plan for conversion from an opioid agonist to buprenorphine
Opioids

General Overview
Opioid History

The opium poppy was cultivated as early as 3400 BC in Mesopotamia. Modern prescription opioids bind to opioid receptors in the CNS and peripheral tissues.

- Indication: moderate to severe pain that does not respond to non-opioids

Role in therapy

- Acute (trauma, post operative pain)
- Breakthrough pain
- Cancer pain
- Chronic non cancer pain

CDC guidelines

- Limited evidence for use of opioids

Opioid Receptors

4 Types of Opioid Receptors

• Mu
  o $\mu_1$ - analgesia
  o $\mu_2$ - sedation, vomiting, respiratory depression, physical dependence, euphoria, anorexia, urinary retention

• Kappa

• Delta

• ORL-1

# Opioid Receptor and Analgesic Effects

<table>
<thead>
<tr>
<th>Full-Agonist</th>
<th>Mu1 and Mu2</th>
<th>Delta</th>
<th>Kappa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>Agonist</td>
<td></td>
<td>Weak agonist</td>
</tr>
<tr>
<td>Codeine</td>
<td>Weak agonist</td>
<td>Weak agonist</td>
<td>Weak agonist</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Agonist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meperidine</td>
<td>Agonist</td>
<td>Agonist</td>
<td></td>
</tr>
<tr>
<td>Methadone</td>
<td>Agonist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antagonist</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naloxone</td>
<td>Antagonist</td>
<td>Weak antagonist</td>
<td>Antagonist</td>
</tr>
<tr>
<td>Naltrexone</td>
<td>Antagonist</td>
<td>Weak antagonist</td>
<td>Antagonist</td>
</tr>
</tbody>
</table>

Definitions Relating to Opioid Use

Tolerance
A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of drugs effects over time. As a result, patient must consume increasingly higher doses to achieve same effect

Physical and Psychological Dependence
A state of adaptation that is manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of drug

The Opioid Epidemic

CDC reports nearly 840,000 overdose deaths since 1999

• The first wave of deaths began with increased prescribing of opioids in the 1990s
• 80% of heroin users started with prescription opioids

Drug overdose deaths involving synthetic opioids and methamphetamine have shifted geographically.

• From 2018 to 2019, the largest increase in death rates involving synthetic opioids occurred in the West (67.9%).
• The largest increase in death rates involving psychostimulants occurred in the Northeast (43.8%).

https://www.cdc.gov/drugoverdose/epidemic/index.html
https://www.opidemic.org/
Figure 3. Age-adjusted rates of drug overdose deaths involving opioids, by type of opioid: United States, 1999–2019

NOTES: Drug overdose deaths are identified using the international Classification of Diseases, 10th Revision (ICD–10) underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Drug overdose deaths involving selected drug categories are identified by specific multiple-cause-of-death codes: heroin, T40.1; natural and semisynthetic opioids, T40.2; methadone, T40.3; and synthetic opioids other than methadone, T40.4. Deaths involving more than one opioid category (e.g., a death involving both methadone and a natural or semisynthetic opioid) are counted in both categories. Natural and semisynthetic opioids include drugs such as morphine, oxycodone, and hydrocodone; and synthetic opioids other than methadone include drugs such as fentanyl, fentanyl analogs, and tramadol. The percentage of drug overdose deaths that identified the specific drugs involved varied by year, ranging from 75%–78% from 1999 through 2013 and increasing from 81% in 2014 to 94% in 2019. Access data table for Figure 3 at: https://www.cdc.gov/nchs/data/databriefs/db294-tables-508.pdf#3.

Buprenorphine

General Overview
Pharmacology of Buprenorphine

Semisynthetic opioid developed in 1966

Mechanism of Action
• Partial agonist at the µ opioid receptor
• Antagonist at κ receptors
• Very high affinity for receptors and slow dissolution rate

Metabolism
• Metabolized to active metabolite (norbuprenorphine) by CYP3A4
• Bioavailability: oral 10%, buccal 45-65%, sublingual 29%, patch 15%

Elimination
• Feces 70%, urine 30%
• Half life: buccal 27 hrs, sublingual 37 hrs, patch 26 hrs
Pharmacology of Buprenorphine

Mechanism of Action
• Low to moderate doses can achieve the same analgesia compared to a full μ opioid agonist
• “Ceiling effect” of respiratory depression
• Antagonist at k receptors - possible mechanism for reduced hyperalgesia
• Lower doses still demonstrate effective analgesia (even if lower % of receptors occupied)
• Higher doses are useful in opioid use disorder (OUD), because it can block other opioid agonists from receptor

Metabolism
• Due to differences in bioavailability, be careful if interchanging between dosage formulations

Elimination
• Low renal elimination
• Inherently long acting, no need for novel formulations
• At lower doses (such as transdermal for buccal formulations), urine drug screens may not detect buprenorphine or metabolites

Ceiling Effect of Respiratory Depression

Respiratory responses

- Buprenorphine 0.2 mg
- Buprenorphine 0.4 mg

Ventilation ± sd (litre min⁻¹)

Time (min)

Analgesia

- Buprenorphine 0.2 mg
- Buprenorphine 0.4 mg

Pain tolerance ± sd (AmA)

Time (min)

Benefits of Buprenorphine

Compared to full opioid agonists

• Ceiling effect for respiratory depression while maintaining analgesia
• Less development of tolerance
• Ease of use in renal impairment and elderly
• Longer acting without novel formulations
• Also
  • Less rewarding effects
  • Less effect on hypogonadism
  • Less constipation
  • Not associated with serotonin syndrome

Ehrlich AT. Pain Manag. 2019
<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage Form</th>
<th>Indication</th>
<th>Strength(s)</th>
<th>General Cost (Select Health)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>IV, IM</td>
<td>Analgesia</td>
<td>0.3 mg/ml</td>
<td>Generic ~$12/mL (medical benefit)</td>
</tr>
<tr>
<td>(Buprenex®)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Buccal</td>
<td>Analgesia</td>
<td>75mcg-900mcg</td>
<td>Brand ~$6-$14/film (preferred brand)</td>
</tr>
<tr>
<td>(Belbuca™)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Sublingual</td>
<td>OUD, Analgesia</td>
<td>2mg, 8mg</td>
<td>Generic ~$2/tab (non-preferred)</td>
</tr>
<tr>
<td>(Subutex®)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>Transdermal</td>
<td>Analgesia</td>
<td>5 mcg/hr, 7.5 mcg/hr, 10 mcg/hr, 15</td>
<td>Brand ~$81-$215/patch (not covered on formulary)</td>
</tr>
<tr>
<td>(Butrans®)</td>
<td></td>
<td></td>
<td>mcg/hr, 20 mcg/hr</td>
<td>Generic ~$70-$166/patch (non-preferred generic, covered without</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>step or prior auth)</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>SubQ</td>
<td>OUD</td>
<td>100 mg/0.5ml, 300 mg/1.5ml</td>
<td>Brand ~$1,600/month (medical benefit, prior auth)</td>
</tr>
<tr>
<td>(Sublocade®)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>SubQ</td>
<td>OUD</td>
<td>74.2mg</td>
<td>Brand ~$5,200/implant (medical benefit, prior auth)</td>
</tr>
<tr>
<td>(Probuphine®)</td>
<td>Implant</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Buprenorphine/Naloxone Formulations

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage Form</th>
<th>Indications</th>
<th>Strength(s)</th>
<th>General Cost (Select Health)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine/naloxone (Suboxone®)</td>
<td>Sublingual film</td>
<td>OUD</td>
<td>2 mg/0.5 mg, 4 mg/1 mg, 8 mg/2 mg, 12 mg/3 mg</td>
<td>Brand ~$5-$18/film Generic ~$2-$12/film</td>
</tr>
<tr>
<td>Buprenorphine/naloxone (Zubzolv®)</td>
<td>Sublingual tablet</td>
<td>OUD</td>
<td>0.7 mg/0.18 mg, 1.4 mg/0.36 mg, 2.9 mg/0.71 mg, 5.7 mg/1.4 mg, 8.6 mg/2.1 mg, 11.4 mg/2.9 mg</td>
<td>Brand ~$5-$18/tab (not covered on formulary)</td>
</tr>
<tr>
<td>Buprenorphine/naloxone (Bunavail®)</td>
<td>Buccal film</td>
<td>OUD</td>
<td>2.1 mg/0.3 mg, 4.2 mg/0.7 mg, 6.3 mg/1 mg</td>
<td>No longer available</td>
</tr>
</tbody>
</table>

Buprenorphine Use in Substance Abuse Disorder

Suboxone approved in 2002 for treatment of opioid addiction

• Prior to its approval, opioid addiction was most commonly treated with methadone. Methadone can be dispensed only in a limited number of clinics that specialize in addiction treatment.

Suboxone was the first opioid available under the Drug Abuse Treatment Act of 2000 (DATA) for the treatment of [opioid] dependence that can be prescribed in a doctor’s office.

https://www.samhsa.gov/medication-assisted-treatment/statutes-regulations-guidelines
Who Can Prescribe Buprenorphine?

Depends on the indication

OUD, per DATA 2000 & SUPPORT Act 2018:

• Requires special waiver with ‘X’ number issued by the DEA
  o Up to 30 patients without additional training
  o Up to 100 patients in year one, then up to 275 patients with additional training

Pain:

• Does not require XDEA license
• Prescribed off-label depending on formulation

https://www.samhsa.gov/medication-assisted-treatment/statutes-regulations-guidelines
https://www.samhsa.gov/medication-assisted-treatment/become-buprenorphine-waivered-practitioner
Who Can Prescribe Buprenorphine?

Punch line, must document on the prescription:

• Indication for buprenorphine
• DEA # and XDEA # if for OUD

https://www.samhsa.gov/medication-assisted-treatment/become-buprenorphine-waivered-practitioner
https://www.hhs.gov/about/news/2021/01/14/hhs-expands-access-to-treatment-for-opioid-use-disorder.html
Conversion to Buprenorphine

CDC removed buprenorphine in the 2017 conversion factors

- The conversion factors for drugs prescribed or provided as part of MAT for OUD should not be used to benchmark against dosage thresholds meant for opioids prescribed for pain
- These buprenorphine products, as partial opioid agonists, are not expected to be associated with overdose risk in the same dose-dependent manner as doses for full agonist opioids

<table>
<thead>
<tr>
<th>Opioid (strength units)</th>
<th>MME Conversion Factor (2016)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine (mg)</td>
<td>1</td>
</tr>
<tr>
<td>Oxycodone (mg)</td>
<td>1.5</td>
</tr>
<tr>
<td>Buprenorphine film/tablet (mg)</td>
<td>30</td>
</tr>
<tr>
<td>Buprenorphine patch (mcg/hr)</td>
<td>12.6</td>
</tr>
<tr>
<td>Buprenorphine film (mcg)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Active Learning Question

When prescribing buprenorphine, regardless of indication/dose/quantity, providers must demonstrate an X DEA number on the prescription.

• True
• False
Active Learning Question

As the dose of buprenorphine increases the risk of respiratory depression also rises? (as seen in full opioid agonists)

• True
• False
Buprenorphine

Use in Chronic Pain
Buprenorphine Use in Chronic Pain

Goal for Use:

- Manage pain symptoms and encourage ADL
- Completely replace full opioid agonists
- Reduce risk and/or symptoms of OUD
- Protective ceiling effect
# Sublingual Buprenorphine for Chronic Pain

## Systematic Review

<table>
<thead>
<tr>
<th>Studies and number of participants</th>
<th>10 studies (n = 1190 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>9 observational studies</td>
</tr>
<tr>
<td></td>
<td>1 RCT</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Buprenorphine SL (dose range 0.4 mg to 32 mg and not reported)</th>
<th>Comparator:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>None, TD buprenorphine (1 study), morphine (1 study)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>• Due to heterogeneity of studies pooling of results and meta-analysis not possible</td>
</tr>
<tr>
<td>• All studies reported SL buprenorphine demonstrated some effectiveness</td>
</tr>
<tr>
<td>• Majority low quality observational studies</td>
</tr>
</tbody>
</table>

| Safety/common side effects | Nausea, vomiting, confusion, dizziness, sedation, constipation and sweating |

**RCT** = randomized controlled trial; **SL** = sublingual; **TD** = transdermal

### Chronic Pain using various buprenorphine formulations

#### Systematic Review

<table>
<thead>
<tr>
<th>Studies and number of participants</th>
<th>25 RCTs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants ≥ 18 years with chronic pain (≥ 3 months) of any etiology (and not OUD)</td>
<td>Comparator: placebo, short-acting or long-acting opioid agonists</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Buprenorphine/naloxone (1 study)</th>
<th>Buprenorphine SL (3 studies)</th>
<th>Buprenorphine IV (3 studies)</th>
<th>Buprenorphine buccal (3 studies)</th>
<th>TD (15 studies)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Pain diagnosis included CLBP, osteoarthritis, neuropathy, and cancer-related pain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>14 studies demonstrated clinically significant benefit with buprenorphine in the management of chronic pain:</td>
</tr>
<tr>
<td></td>
<td>• 1/6 sublingual and intravenous buprenorphine, 1 study sublingual buprenorphine/naloxone study, 2/3 studies of buccal buprenorphine, and 10/15 studies for TD buprenorphine showed significant reduction in pain against a comparator.</td>
</tr>
</tbody>
</table>

| Safety/common side effects | No serious adverse effects were reported in any of the studies |

CLBP = chronic low back pain; IV = intravenous; OUD = opioid use disorder; RCT = randomized controlled trial; SL = sublingual; TD = transdermal

## Sublingual Buprenorphine for Chronic Pain

### Retrospective Cohort Study

<table>
<thead>
<tr>
<th>Trial Design</th>
<th>Retrospective Cohort (n = 104)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Interventions</strong></td>
<td>Conversion from full opioid agonist to Buprenorphine SL</td>
</tr>
<tr>
<td></td>
<td>• Average pre-conversion MME 180</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>After 2 months:</td>
</tr>
<tr>
<td></td>
<td>• Mean pain scores decreased by 2.3 points on a 1-10 scale (P&lt;0.001)</td>
</tr>
<tr>
<td></td>
<td>• 100-199 MME experienced greatest decrease of 2.7 points</td>
</tr>
<tr>
<td></td>
<td>• 200-299 MME experienced decrease of 2 points</td>
</tr>
<tr>
<td></td>
<td>• &gt;400 MME had smallest decrease of 1.1 points</td>
</tr>
<tr>
<td><strong>Safety/Common side effects</strong></td>
<td>Well tolerated and few side effects reported</td>
</tr>
</tbody>
</table>

# Transdermal Buprenorphine and Fentanyl

<table>
<thead>
<tr>
<th>Trial design</th>
<th>Retrospective study utilizing data from Germany database</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Interventions</strong></td>
<td>Patients with cancer (n = 446) and non-cancer pain (n = 448) on medication for ≥ 3 months</td>
</tr>
</tbody>
</table>
| **Outcomes** | - Mean % increase in dosages over treatment duration were significantly higher in TD fentanyl group ($P < 0.05$)  
- Differences were even greater for the mean percentile intraindividual increases per day:  
  • Total 0.42% and 0.17% for cancer patients taking TD fentanyl and TD buprenorphine, respectively  
  • corresponding values were 0.25% and 0.09% in noncancer patients ($P < 0.001$) |

Buprenorphine vs Methadone

<table>
<thead>
<tr>
<th>Trial design</th>
<th>Randomized open label trial (n = 54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective</td>
<td>Compare methadone and buprenorphine for analgesia: Randomized to receive methadone (10 to 60 mg/day) or buprenorphine/naloxone (16/4 mg daily) for 6 months</td>
</tr>
<tr>
<td>Patient population</td>
<td>Adults with chronic non-cancer pain and addiction to prescription opioids</td>
</tr>
</tbody>
</table>
| Results             | Average daily dose: methadone 29 mg and Bup/naloxone 14.93/3.73 mg  
Both treatments resulted in analgesia and did not differ between groups.  
At 6 months, 26 (48.1%) participants who remained in the study noted a 12.75% reduction in pain ($P = 0.043$).  
Reported illicit opioid use occurred in 5 patients of the buprenorphine group and 0 in the methadone ($P = 0.039$). |

Buprenorphine for Use for Chronic Pain

Consider use if:

- Failed attempts to wean down or off opioids
- Overusing opioid Rx
- Preoccupation with use disrupting patient ADL
- Using high MME (> 90 mg/day)
- Any other evidence of OUD
- Impaired control or social ability, risky use, demonstrated dependence or tolerance
- Desire for protective ceiling effect

ADL = activities of daily living; MME = Milligram morphine equivalent; OUD = opioid use disorder
Buprenorphine

Conversion to Buprenorphine
Conversion to Buprenorphine

Label dosing for Buprenorphine patches/buccal film for pain

• Taper opioids to ≤30 MME
• Stop opioids
• Based on previous opioid dose, start
  o <30 MME: 75 mcg buccal film once daily or every 12 hours or 5 mcg patch
  o 30 to 89 MME: 150 mcg buccal film every 12 hours or 10 mcg patch
  o 90 to 160 MME: 300 mcg buccal film every 12 hours or 20 mcg patch
  o >160 MME: may not provide adequate analgesia

Conversion to Buprenorphine

Label dosing for Buprenorphine SL tabs for OUD:

• Induction:
  o Stop all opioids
  o Upon clear signs of withdrawal, give 2-8 mg SL
  o Titrate dose slowly by 2-4 mg until on stable dose for 24 hours
• Maintenance: 8-24 mg/day (split BID)

Conversion to Buprenorphine

“Micro dosing Buprenorphine”

• Small doses throughout the day and titrating over several days
  o Most report using partial SL tablets or films
    ▪ Many use transdermal patches, buccal formulations, or a combination or products
    ▪ Some start with patch, then start low SL doses on day 2
  o May be outpatient and over multiple days

• Although most discontinue full opioid agonists before initiation, numerous studies report starting titration before
  o Most cross tapers were used for OUD with a predetermined target dose

Conversion to Buprenorphine

Pearls from Layton Chronic Pain Management Clinic

• Consider transitioning to buprenorphine rapidly similar to OUD
• Attempt to taper down on opioid dose prior to conversion as possible
• Ensure all opioids are stopped and anticipate withdrawal symptoms before starting buprenorphine
  o Stop current opioids at least 24 hours before conversion
    ▪ Longer for methadone
  o Ensure withdrawal to prevent precipitated withdrawal from buprenorphine
  o Provide supportive therapies for withdrawal
• Observation following initial dose for at least 4-6 hours
  o Do not allow patient to drive until on stable dose
Patient Case

39-year-old female, with extensive history of chronic pain associated with chronic demyelinating polyneuropathy

• Had multiple chronic pain providers over several years
  ○ History of multiple opioid and non-opioid medications
• Complains of daily pain that effects activities of daily life
• Presents on methadone 75 mg three times per day
  ○ MME ~2,700
  ○ Recent hx of dose up to 160 mg three times per day (MME ~5,760)
• Currently reports taking more than prescribed to control pain
Patient Case - Question

We discussed a plan to convert to buprenorphine. What factors in her case support this plan? (Select all that apply)

a) Clear evidence of opioid use disorder
b) Current disruption of activities of daily life
c) Failed other therapies (opioid and non-opioid)
d) High MME
After an extensive discussion, she agreed to conversion to buprenorphine. What steps should be taken to prepare for the transition? (Select all that apply)

a) Taper current opioid to the lowest tolerated dose
b) Stop methadone 24 hours prior to transition
c) Ensure at least mild symptoms of withdrawal
d) Observe for several hours after initial dose
Patient Case

39-year-old female, agreed to conversion to buprenorphine

• Chose to admit to hospital for observed conversion
• Stopped methadone on a Saturday
• Complained of withdrawal sx by Monday
  o Diarrhea, nausea, generalized pain, lacrimation
• Admitted to hospital on Monday afternoon for withdrawal
Patient Case

39-year-old female, conversion to buprenorphine

Hospitalization

• Supportive medications for acute withdrawal
  o Clonidine, lorazepam, hydroxyzine, promethazine
• Non-opioid medications for pain
  o Duloxetine, pregabalin, baclofen, APAP
• Long-acting and PRN short-acting opioid agonists for breakthrough until methadone completely out of system
  o Oxycodone ER, hydromorphone, morphine
Patient Case

39-year-old female, conversion to buprenorphine

Hospitalization

• Stopped all opioids on Thursday AM
• Start buprenorphine 8mg SL Thursday PM
  o Per pain/withdrawal, gave additional 4mg dose that night
• Discharged Saturday stable on 8mg buprenorphine Q8hr
  o Reported pain as controlled as previously on methadone
Buprenorphine

Buprenorphine and Procedures
Buprenorphine and Procedures

Currently no consensus guidelines describing optimal management

Many institutions develop internal protocols

• Key principles of protocols
  o Offer multimodal pain management
  o Pre and post procedure planning

• Key factors to consider
  o Is the procedure elective or emergent
  o What level of pain is expected from the procedure
  o Indication for buprenorphine
  o Current dose of buprenorphine

Buprenorphine and Procedures

General considerations for surgical event:
Many institutions develop internal protocols

• Communicate with patients’ prescribing physician
• Optimize non-opioid analgesic therapies
• Expect higher than usual doses of full opioid agonists if used in combination with buprenorphine
• Doses of buprenorphine maybe increased

Buprenorphine and Procedures

When to restart buprenorphine if stopped for procedure?

• Many protocols recommend 1-3 days or at least by discharge
• Careful coordination between surgeons and outpatient managing provider
• ASAM recommends continuing buprenorphine for OUD
  o Increasing buprenorphine dose and frequency
  o Adding short acting full agonist opioid

Patient Maintained on Buprenorphine Presents for Surgical Event (a)

PREOPERATIVE MANAGEMENT

- PLAN with the outpatient providing prescriber and other applicable specialists.
- In almost all cases, maintain buprenorphine at the preoperative dose.
- In all cases, optimize multimodal analgesia (b).

Is the patient in the rare group meeting special consideration criteria for tapering? (c)

- no (most cases)
  - MAINTAIN buprenorphine at preoperative dose
- yes
  - REVIEW dose reduction advisory (c). Tapering is a rare occurrence.
INTRAOPERATIVE MANAGEMENT

- ADMINISTER multimodal analgesia.
- UTILIZE regional analgesia and/or Acute Pain Services (APS) where available.

Is pain adequately controlled WITHOUT full-agonist opioids?

- yes
  - PROCEED to postoperative instruction
- no
  - UTILIZE short-acting full agonist opioids

**Caution:** The use of full opioid agonists in patients who have been tapered increases the risk of respiratory depression, overdose, and other dangers.
Intermountain Perioperative Management

POSTOPERATIVE MANAGEMENT

- Pain controlled without full agonist opioids
  - Implement usual monitoring
    - Standard PACU monitors

- Full agonist opioids USED
  - Implement continuous monitoring
    - Pulse oximetry
    - Respiratory rate via capnography (when available)
  - If dose was tapered (c)
  - RESUME preoperative dose of buprenorphine 1-3 days post-surgery as patient transitions off all other opioids

- Dose tapered AND full agonist opioids USED
Patient Case Cont.

39-year-old female, now stable on 32 mg buprenorphine per day
Requires extensive debridement of past left shoulder arthroplasty
Patient expresses that she is very hesitant to restart opioids

• Current medications for pain or related
  o Buprenorphine-naloxone 8-2mg SL tabs, 2 tabs BID
  o APAP 500mg tabs, 2 tabs TID
  o Baclofen 10mg tabs, 1 tab BID
  o Pregabalin 150mg caps, 1 cap TID
  o Tramadol 50mg tab, 2 tabs Q6Hr PRN
  o Lorazepam 0.5mg tab, 1 tab TID PRN
Patient Case Cont.

39-year-old female, now stable on 32 mg buprenorphine per day

Requires extensive debridement of past left shoulder arthroplasty

All elements must be considered, EXCEPT which of the following?

a) If the procedure planned or emergent
b) Current daily MME due to buprenorphine
c) Current buprenorphine dosing and pain levels
d) Anticipated pain level of procedure
Patient Case Cont.

39-year-old female, now stable on 32 mg buprenorphine per day
Requires extensive debridement of past left shoulder arthroplasty

• What recommendations would you give to the managing provider and surgeon?
Patient Case Cont.

39-year-old female, elected to avoid all opioid medications after procedure and to continue buprenorphine before and after procedure

• Prior to procedure
  o Optimized non-opioid medications
  o Tapered buprenorphine to 16mg daily (half of current dose) over 2.5 weeks

• During procedure received midazolam, fentanyl, lidocaine, propofol, meperidine, ketamine, bupivacaine, and hydromorphone

• After procedure
  o Ketorolac
  o Increased frequency of buprenorphine while admitted
  o Upon discharge, titrated back to previous dose/frequency
Buprenorphine

Overdose and Naloxone
# Buprenorphine and Naloxone Used for Overdose

<table>
<thead>
<tr>
<th>Trial design</th>
<th>Placebo controlled, Double blind</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective</td>
<td>Ability of naloxone to reverse respiratory depression produced by buprenorphine</td>
</tr>
<tr>
<td>Patient population</td>
<td>Healthy volunteers without history of illicit drug use or mental disease (n = 67)</td>
</tr>
<tr>
<td>Results</td>
<td>- IV naloxone dose of 0.8 mg had no effect on respiratory depression from buprenorphine</td>
</tr>
<tr>
<td></td>
<td>- Increasing doses given over 30 min produced full reversal in dose range of 2 to 4 mg naloxone</td>
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<tr>
<td></td>
<td>- Further increasing dose of naloxone (≥ 5mg) caused decline in reversal activity</td>
</tr>
<tr>
<td>Recommendation</td>
<td>Naloxone bolus doses of 2 to 3 mg, followed by continuous infusion of 4 mg/hour caused full reversal in 40 to 60 min</td>
</tr>
</tbody>
</table>

Active Learning Question

Do you consider recommending a naloxone emergency kit for a patient with a prescription for Suboxone® 8mg/2mg TID for pain?

a) Yes

b) No
Key Points on Buprenorphine for Chronic Pain

• Buprenorphine is an opioid with a unique mechanism of action which can produce analgesia and has a better safety profile than full opioid agonists
• Can be very useful for patients who show any signs of OUD
• When converting from full opioid agonists
  o Taper down to lowest dose possible
  o Stop all opioids and wait for withdrawal sx before starting buprenorphine
  o Observe patient after first dose
• Ensure proper planning for any procedure that may cause acute pain
Bibliography/References


National Center for Injury Prevention and Control. CDC compilation of benzodiazepines, muscle relaxants, stimulants, zolpidem, and opioid analgesics with oral morphine milligram equivalent conversion factors, 2016 version.

National Center for Injury Prevention and Control. CDC compilation of benzodiazepines, muscle relaxants, stimulants, zolpidem, and opioid analgesics with oral morphine milligram equivalent conversion factors, 2017 version.


The Opioid Epidemic

Utah

• 5 Utahns die every week from opioid overdose
• In 2019, Utah ranked 27th for drug overdose mortality
  o 571 Utahns died in 2019
  o In 2015 Utah ranked 7th highest in drug poisoning deaths
  o One of only nine states to observe a decrease in opioid overdose deaths from 2016 to 2017
• Drug poisoning deaths have outpaced deaths due to firearms, falls, and motor vehicle crashes

https://www.opidemic.org/
Intermountain Project ECHO

Pain Management

Buprenorphine for Chronic Pain

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