Buprenorphine/naloxone in the ED

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Dr. Jodie Turner

November 25th 2021
We respectfully acknowledge the land on which we work is the unceded traditional territory of the Coast Salish Peoples, including the traditional territories of x̕w̓μəθkwəy̓əm (Musqueam), Skwxwú7mesh (Squamish), Sn̓ən̓eílməxʷ (Snuneymuxw) and Səl̓ílwətaɬ (Tsleil-Waututh) Nations.
Disclaimer

Some of the protocols described in this presentation have been developed in response to the ongoing opioid crisis due to fentanyl in the illicit drug supply, and may not be represented in current BCCSU Guidelines.

This includes innovative and novel approaches specific to emergency settings that are based on clinical experience. There is currently little evidence or research into the effectiveness of some of these protocols, therefore clinical judgement is advised.
Housekeeping

• This webinar is interactive! You can answer by:
  – Using the "raise hand" function
  – Posting in the chat
• If you feel comfortable, please turn on your cameras when participating
• This sessions will be recorded
• Cases are based on real clinical scenarios, but have been adapted for simplicity
• Any missed questions will be answered in a round up email post webinar
• We will stay after the webinar to continue the discussion for those who are interested
• For a more in depth review, please see learning materials available on our platform shortly: https://www.bccsu.ca/edcare/
Facilitators

- Elder Wayne Seward
- Aimee Chalifoux
- Dr. Jodie Turner
- Dr. Anne Sutherland
Learning Objectives

By the end of this webinar you will be able to:

1. Describe an approach to buprenorphine/naloxone induction, including selection of protocol
2. Confidently initiate and support a microinduction in various settings
3. Identify and treat precipitated withdrawal
4. Assess patients for missed doses of buprenorphine/naloxone
5. Manage atypical inductions
Webinar Outline

- Welcoming Prayer
- Case discussion (4-5) with review of clinical pearls
- Q+A
- Closing Prayer
Welcome
Case 1

• 32 male presents to your ED during an evening shift with right arm purulent cellulitis.
• He has a history of opioid use disorder, injecting an 8 ball (3.5 g) of fentanyl daily.
  – Hist last use was 12 hours prior.
  – He was on buprenorphine/naloxone 1 year ago.
  – He denies any other substances.
• He has no other past medical history and has no regular medications.
• He wants to stop using fentanyl but feels helpless given he’s tried several times before on his own.
Case 1

“Have you thought about buprenorphine/naloxone?”
Case Discussion

• How do you provide informed consent around buprenorphine/naloxone?
  – Induction method?
  – Continuation?

• What is your approach to discussing the risk of precipitated withdrawal?

• What are the different types of induction you can offer?
  – How do you select the best fit for your patient?
Approach to Buprenorphine Induction

• Your patient should understand:
  – The induction process
  – Expectations with maintenance on buprenorphine/naloxone
  – The risk of precipitated withdrawal
• Agree on how to treat precipitated withdrawal before the induction
• When deciding on the type of induction
  – Always assess for standard induction first
  – Ask what is feasible for the patient
Is the patient in active withdrawal? COWS > 12 (Consider 16-18 if +fentanyl use) 24-48 hours since last use or can wait this time?

1. Standard induction (ED or Community)
2. Microinduction
<table>
<thead>
<tr>
<th>Resting Pulse Rate:</th>
<th>GI Upset: over last 1/2 hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measured after patient is sitting or lying for one minute</td>
<td>0 no GI symptoms</td>
</tr>
<tr>
<td>0 pulse rate 80 or below</td>
<td>1 stomach cramps</td>
</tr>
<tr>
<td>1 pulse rate 81-100</td>
<td>2 nausea or loose stool</td>
</tr>
<tr>
<td>2 pulse rate 101-120</td>
<td>3 vomiting or diarrhea</td>
</tr>
<tr>
<td>4 pulse rate greater than 120</td>
<td>5 multiple episodes of diarrhea or vomiting</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sweating: over past 1/2 hour not accounted for by room temperature or patient activity.</th>
<th>Tremor observation of outstretched hands</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 no report of chills or flushing</td>
<td>0 no tremor</td>
</tr>
<tr>
<td>1 subjective report of chills or flushing</td>
<td>1 tremor can be felt, but not observed</td>
</tr>
<tr>
<td>2 flushed or observable moistness on face</td>
<td>2 slight tremor observable</td>
</tr>
<tr>
<td>3 beads of sweat on brow or face</td>
<td>4 gross tremor or muscle twitching</td>
</tr>
<tr>
<td>4 sweat streaming off face</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Restlessness Observation during assessment</th>
<th>Yawning Observation during assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 able to sit still</td>
<td>0 no yawning</td>
</tr>
<tr>
<td>1 reports difficulty sitting still, but is able to do so</td>
<td>1 yawning once or twice during assessment</td>
</tr>
<tr>
<td>3 frequent shifting or extraneous movements of legs/arms</td>
<td>2 yawning three or more times during assessment</td>
</tr>
<tr>
<td>5 unable to sit still for more than a few seconds</td>
<td>4 yawning several times/minute</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pupil size</th>
<th>Anxiety or Irritability</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 pupils pinned or normal size for room light</td>
<td>0 none</td>
</tr>
<tr>
<td>1 pupils possibly larger than normal for room light</td>
<td>1 patient reports increasing irritability or anxiousness</td>
</tr>
<tr>
<td>2 pupils moderately dilated</td>
<td>2 patient obviously irritable or anxious</td>
</tr>
<tr>
<td>5 pupils so dilated that only the rim of the iris is visible</td>
<td>4 patient so irritable or anxious that participation in the assessment is difficult</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bone or Joint aches If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored</th>
<th>Gooseflesh skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 not present</td>
<td>0 skin is smooth</td>
</tr>
<tr>
<td>1 mild diffuse discomfort</td>
<td>3 piloeruction of skin can be felt or hairs standing up on arms</td>
</tr>
<tr>
<td>2 patient reports severe diffuse aching of joints/muscles</td>
<td>5 prominent piloerrection</td>
</tr>
<tr>
<td>4 patient is rubbing joints or muscles and is unable to sit still because of discomfort</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Runny nose or tearing Not accounted for by cold symptoms or allergies</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0 not present</td>
<td></td>
</tr>
<tr>
<td>1 nasal stuffiness or unusually moist eyes</td>
<td></td>
</tr>
<tr>
<td>2 nose running or tearing</td>
<td></td>
</tr>
<tr>
<td>4 nose constantly running or tears streaming down cheeks</td>
<td></td>
</tr>
</tbody>
</table>

|  | Total Score |  |
|----------------|--------------|
|  | The total score is the sum of all 11 items |

<table>
<thead>
<tr>
<th></th>
<th>Initials of person</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>completing assessment:</td>
</tr>
</tbody>
</table>
Case 1 – Discharged Home

• You prescribe a 7 day course of antibiotics.
• The patient doesn’t feel he can wait 24-48 hours in withdrawal for a standard induction.
• He wonders about something he heard from his friends – a microinduction?
Case Discussion

- What is a microinduction and how does it work?
- How do you decide if someone is appropriate for a microinduction?
- What are key things to explain to your patient about this approach?
Buprenorphine Microinduction

• Incremental doses of buprenorphine over days = small shifts of full agonist off the receptor
  – Below “threshold” for precipitated withdrawal
  – No wait or withdrawal required prior to initiation

• No standard protocol
  – Variability in literature and amongst providers
  – Duration: 3-10+ days
  – Frequency: BID to q3-4h dosing
Microinduction Key Concepts

1. Less withdrawal, but not absence of withdrawal
2. Risk of precipitated withdrawal is less but not zero
3. Aim = prevent symptoms, not alleviate
4. Until reach maintenance dose patients will continue to:
   – Be at risk for overdose
   – Experience withdrawal
5. Microinductions are not necessarily easy for patients = take time for discharge instructions
Case 1 – Discharged Home

• Your patient agrees to proceed with a microinduction and is ready to go home.
Case Discussion

• What protocols are available, and which one do you choose?
• How can you increase your patient’s success with microinductions?
• What do you discuss in your discharge instructions?
## Example Protocol – BID dosing

<table>
<thead>
<tr>
<th>Day</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>0.5mg BID</td>
</tr>
<tr>
<td>Day 2</td>
<td>1mg BID</td>
</tr>
<tr>
<td>Day 3</td>
<td>2mg BID</td>
</tr>
<tr>
<td>Day 4</td>
<td>3mg BID</td>
</tr>
<tr>
<td>Day 5</td>
<td>4mg BID</td>
</tr>
<tr>
<td>Day 6</td>
<td>12mg daily</td>
</tr>
<tr>
<td>Day 7</td>
<td>8mg BID</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
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<th>Dose</th>
</tr>
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<td>1mg BID</td>
</tr>
<tr>
<td>Day 3</td>
<td>2mg BID</td>
</tr>
<tr>
<td>Day 4</td>
<td>3mg BID</td>
</tr>
<tr>
<td>Day 5</td>
<td>4mg BID</td>
</tr>
<tr>
<td>Day 6</td>
<td>6mg BID</td>
</tr>
<tr>
<td>Day 7</td>
<td>8mg BID</td>
</tr>
</tbody>
</table>
## Example Protocol – QID Dosing

<table>
<thead>
<tr>
<th>Day</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>0.5mg QID</td>
</tr>
<tr>
<td>Day 2</td>
<td>1mg QID</td>
</tr>
<tr>
<td>Day 3</td>
<td>2mg QID</td>
</tr>
<tr>
<td>Day 4</td>
<td>3mg QID</td>
</tr>
<tr>
<td>Day 5</td>
<td>12-16mg daily</td>
</tr>
</tbody>
</table>
Discharging Patients with a Microinduction

• Provide medications to treat withdrawal dispensed from ED or Rx
  – Non opioids: acetaminophen, NSAIDs, antiemetics, clonidine, quetiapine ...
  – Some providers with expertise may prescription full agonist opioid concurrently

• Buprenorphine/naloxone – 2 options:
  – Doses to go from ED:
    • 0.5mg x 6 doses starter pack with follow up
    • Full blister pack
  – Prescription for microinduction to fill at pharmacy
### Prescription Example

--- BC CONTROLLED PRESCRIPTION FORM ---

**Patient Name**:  
**Address**: 123 Street, Vancouver, BC  
**Date of Birth**: 25 11 1989

**Drug Name and Strength**: Buprenorphine/Naloxone

**Dispense all as crises, please blister pack**  
**Quantity (in units)**: FORTY NINE MG  
**Numerical**: 49 MG  
**Alpha**: V

**Total Daily Dose**: 0 mg/day  
**Number of Days per Week of Daily Witnessed Ingestion**: 0  
**Numerical**: 0  
**Alpha**: Z

**Directions for Use**: Indication for Therapy, or Special Instructions  
Dispense all as crises, please blister pack  
Day 1: 0.5 mg SL BID  
Day 2: 1 mg SL BID  
Day 3: 2 mg SL BID  
Day 4: 3 mg SL BID  
Day 5: 4 mg SL BID  
Day 6: 6 mg SL BID  
Day 7: 8 mg SL BID

**Prescriber’s Signature**:  
**Prescriber ID**: 11551 91  
**Address**: KUALALAMPUDDAIPARISUDBL, BC  
**Prescriber’s Contact Information**: KUALALAMPUDDAIPARISUDBL, BC  
**Pharmacy Use Only**:  
**Pharmacy Copy - Press hard you are making 2 copies**  
**Printed in British Columbia**  
**Substance Use**
Discharging Patients with a Microinduction

• Discuss ways to treat withdrawal and stay safe
  – Review harm reduction strategies
  – Address treatment of withdrawal
    • Ongoing illicit use
    • Symptomatic management (acetaminophen, clonidine etc)
    • Prescription of full agonist opioid

• Give anticipatory guidance on symptoms (i.e., symptomatic days – 4mg BID)

• Organize follow up for:
  – Ongoing prescriptions (continuation of microinduction or maintenance dose)
  – Reassessment of symptoms or missed doses

• Support in the community (outreach, peers)
Case 1 – Overnight in the ED

• As you are about to discharge the patient, he becomes tachycardic, and febrile. The remainder of his vital signs remain stable.

• You order a dose of IV antibiotics, fluids and place him in an observation unit overnight to be reassessed in the morning for possible discharge.
Case Discussion

• How might your approach change if the patient remains in the ED?
• What are ways you can make your patient more comfortable?
### Example Protocol

<table>
<thead>
<tr>
<th>Day</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.5mg q3h x 8</td>
</tr>
<tr>
<td>2</td>
<td>1mg q3h x 8</td>
</tr>
<tr>
<td>3</td>
<td>8mg daily</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Day</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.5mg q3-4h x 4 doses 1mg q3-4h x 4 doses</td>
</tr>
<tr>
<td>2</td>
<td>2mg q3-4h x 4 doses 3mg q3-4h x 4 doses</td>
</tr>
<tr>
<td>3</td>
<td>12-16mg daily</td>
</tr>
</tbody>
</table>
Buprenorphine Microinduction in Acute Care

• Consider a more rapid induction
  – More support and flexibility with symptom management

• Order IR opioids to address withdrawal symptoms until dose is consolidated
  – Hydromorphone preferred > affinity than morphine
  – Example: hydromorphone 4-6mg po q2h PRN
ASSESSMENT FOR BUPRENORPHINE INDUCTION APPROACH

Are they currently in sufficient withdrawal? Can go enough time without using to be in sufficient withdrawal? IR opioids: 6-12 hours, Fentanyl: 24+ hours

- **YES**
  - Standard induction

- **NO**
  - **Microinduction**
    - **Stable (psychosocial, OUD)?** Can the patient manage QID dosing?
      - **YES**
        - **Time constraints?** Wiling to stay awake overnight? Held overnight in the ED?
          - **YES**
            - Ultra-Rapid Microinduction Q3-4h Dosing
          - **NO**
            - Standard microinduction BID dosing
      - **NO**
        - Rapid Microinduction QID dosing
Case 2

• 28 year old female presents in opioid withdrawal
• She has been smoking 1 g of fentanyl daily x 1 year
  – She has never been on opioid agonist therapy
• She is otherwise healthy, no regular medication
• Her bHCG is negative.
Case 2

• Her last use was 18 hours ago, and her COWS (clinical opiate withdrawal scale) is 15.
• You consent to start a buprenorphine/naloxone standard induction.
• She receives 2mg SL
  – 1 hour later: COWS = 15
• She receives a 2nd 2mg SL
  – COWS = 26
Case Discussion

• Is this precipitated withdrawal?
• How is it differentiated from undertreated withdrawal?
• How can minimize this risk?
• What could affect your COWS scale and make it less reliable?
Precipitated Withdrawal

- Rapid onset, severe withdrawal = within 15-30 minutes
  - VS undertreated withdrawal = onset >1 hour or prior to dose
- Minimize risk by
  - Minimum 24-48 hours since last use with fentanyl
  - Higher COWS threshold
  - Objective symptoms > subjective
- COWS scale can be affected by
  - Concurrent sedative withdrawal (benzo, alcohol)
  - Acute medical illness
  - Psychiatric co-morbidities
Case Discussion

• What is your approach to precipitated withdrawal?
Treatment of Precipitated Withdrawal

- Notify patient of diagnosis and validate symptoms
- Transfer to bed if possible
- Reach out for support (both for provider and patient)
- Confirm approach to treatment
  - Continue induction
  - Pause/delay induction
  - Stop induction
Treatment of Precipitated Withdrawal

• Non opioid pharmacotherapy
  – Analgesia: acetaminophen, NSAIDs
  – Antiemetics: ondansetron, dimenhydrinate
  – Agitation: antipsychotics (quetiapine)
  – Withdrawal: clonidine
  – GI symptoms: loperamide

• Other pharmacotherapy
  – Ketamine
  – Lorazepam (caution due to risk of overdose)
Treatment of Precipitated Withdrawal

- **Continue**: 2mg SL q1-2H until day 1 max or symptom resolve
  - *Off label*: push through doses 8-16mg to max 32mg
- **Pause**: non opioid medications and reassess in a few hours
- **Stop**: treat with opioids (hydromorphone)
Case 2

• You have ruled out precipitated withdrawal in your patient.
• You continue the induction until you reach 16mg.
  – COWS = 13
  – She reports ongoing withdrawal.
Case Discussion

• What is your approach if the patient continues to have symptoms once you’ve reached the max dose on day 1 (12-16mg)?
• What is your max dose of buprenorphine/naloxone during day 1 of a standard induction?
Ongoing Withdrawal Symptoms During Induction

• Rule out withdrawal from other substances
• Rule out acute medical illness
• It is likely safe to go above 12-16mg
  – Retrospective study in US: no cases of respiratory depression with total dose up to 32mg
  – Treat till symptom resolution
  – Consider max dose of 24-32mg
Case 4

• You discharge this patient on 24mg SL daily.
• She returns 2 months later, having missed her appointment for a new prescription due to COVID restrictions.
• She reports her last dose was 3 days ago.
Case Discussion

• What are important questions to ask the patient?
• What dose do you provide the patient?
• When should you consider re-initiation onto buprenorphine/naloxone?
Missed Doses of Buprenorphine

• Abstinent from all other opioids – assess for tolerance loss
  – Doses >8mg
    • ≤ 5 days: no change
    • 6-7 days: 8mg test dose
    • > 7 days: 4mg test dose

• Relapse to opioids – assess for risk of precipitated withdrawal
  – Can they feel the effects of other opioids?
Case 5

- An unknown male is brought by EHS post overdose.
- He receives a total of 1.8mg of naloxone.
- He becomes more alert but remains slightly drowsy.
- He reports he recently relapsed onto opioids 2 months ago after 2 years of abstinence.
  - He has had several overdoses.
- He would like to start buprenorphine/naloxone but does not want to wait for withdrawal.
- You’ve heard of ways they are starting patients on buprenorphine post overdose but aren’t sure if this patient meets criteria.
Case Discussion

• What is the principle behind post overdose buprenorphine start?
• What patients are considered for this approach?
• Which patients are included?
• What are the risks?
Post Overdose Buprenorphine Start

• Based on small case series in US
  – Naloxone doses are higher vs Canada
  – No patient centered outcomes or experiences published

• Theory
  – Naloxone → withdrawal symptoms
  – Affinity at Mu receptor: Buprenorphine > naloxone
  – Increase activation at receptor = symptom relief
  – Buprenorphine long duration of action = prevents other opioids from binding as naloxone wears off
Uncomplicated opioid overdose reversed with naloxone

Are any patient exclusion criteria present?

- Additional sedative or other intoxicant suspected
- Altered mental status, depressed level of consciousness, delirium, or severe mental illness
- Unable to participate and comprehend a discussion of risks and benefits
- Unable to provide informed consent for any reason
- Acute medical illness or severe chronic disease such as infection, heart failure, respiratory distress or chronic disease, renal failure, or liver failure
- Methadone use in the last 48 hours
- Not a candidate for buprenorphine maintenance treatment for any reason

No to all

Yes to any

Is the Emergency Department able to manage respiratory depression or precipitated withdrawal?

No → Excluded

Yes

Is opioid withdrawal present? (COWS > 4)

No

Informed consent provided after discussion of risks and benefits?

Yes → Start Buprenorphine with 4mg Sublingual

Continue buprenorphine titration per local guideline

Yes → Excluded

Fig. 1. Suggested guideline for the administration of buprenorphine after reversal of opioid overdose with naloxone.
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December 14, 2021

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