# Facilitating discontinuation of intravenous opioids by concurrent use of sublingual buprenorphine with rapid microdosing induction:

## A pain management case study

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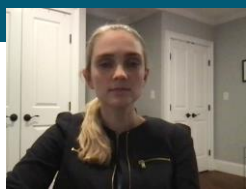


MASSACHUSETTS GENERAL HOSPITAL
DEPARTMENT OF ANESTHESIA, CRITICAL CARE AND PAIN MEDICINE

1

# Overview

- Case description
- Discussion
  - Sublingual buprenorphine as alternative to IV opioid analgesics
  - Concurrent use of buprenorphine & opioid antagonists
  - Initiating buprenorphine in patients receiving full opioid agonists

2

# Disclosures

- None

3

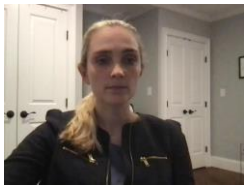
# Case description: PMH, HPI

- 27-year-old female
- BMI 19 kg/m$^2$
- PMH: medically refractory ulcerative colitis, recurrent C. diff colitis, portal vein thrombosis, anxiety, depression
- HPI: presented to ED with nausea, vomiting, severe abdominal pain. POD 10 from laparoscopic J pouch with diverting loop ileostomy at OSH

4

# Case description: Pain history

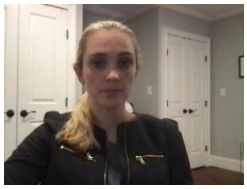
- Analgesic history:
  - Trials of IV & PO hydromorphone, fentanyl patches, ketamine
  - PRN lorazepam
- During previous surgical admission:
  - Required high doses of opioids
  - Poor response to oral agents
- Upon discharge from previous surgical admission: given 10-day taper plan for oral hydromorphone
  - Not able to taper due to inadequate pain relief
  - Marijuana gave some relief



5

# Case description: Early admission

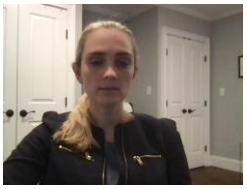
- Admitted to ICU with concerns for sepsis secondary to anastomotic leak
- Drainage scheduled with interventional radiology (IR)
- Made NPO, TPN started for malnutrition
- Multimodal analgesic plan before IR procedure:
  - Scheduled IV acetaminophen
  - PRN IV diazepam
  - Hydromorphone PCA
- Underwent IR procedure



6

# Case description: After IR procedure

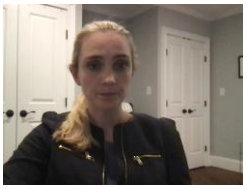
- Post-first IR procedure, diet restarted
  - IV medications transitioned to oral pain medications
- Did not achieve analgesia with PO opioids
  - Needed PRN IV hydromorphone 1mg q3 hours
  - Analgesic response only with IV opioids
  - Intact tablets of PO medications found in ileostomy bag
  - Later refused PO medications given her concern for poor effect



7

# Case description: Starting buprenorphine

- Plan: use sublingual buprenorphine for pain relief & oral and IV opioid analgesics
  - Microdosing induction of buprenorphine
  - Eventually transition off IV opioids
- Patient requested concurrent use of fentanyl patch given positive response in years prior



8

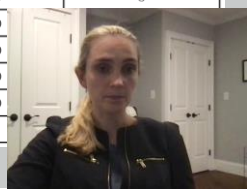
# Case description: Buprenorphine microdosing

- Day 7: Microdosing induction of buprenorphine/naloxone
  - Targeted daily dose of 8 mg buprenorphine
  - Concurrent use of 12 mcg/h transdermal fentanyl patch (dc'd day 9)
- Days 9-25: Morphine PCA added in setting of multiple repeat IR procedures

**Table 1. Daily buprenorphine dose and additional opioid analgesic use**

| Date | Hospital day | Oral opioids | Morphine 24 hours use (mg) | Transdermal fentanyl (mcg/h) | Daily buprenorphine dose (mg)-BID dosing |
|---|---|---|---|---|---|
| October 4 | 7 | Available | Not available | 12 | 1 |
| October 5 | 8 | Available | Not available | 12 | 2 |
| October 6 | 9 | Available | 56* | 12 | 3 |
| October 7 | 10 | – | 84 | 0 | 4 |
| October 8 | 11 | – | 83 | 0 | 4 |
| October 9 | 12 | – | 94 | 0 | 6 |
| October 10 | 13 | – | 60 | 0 | 6 |
| October 11 | 14 | – | 73 | 0 | 6 |
| October 12 | 15 | – | 16 | 0 | 8 |
| October 13 | 16 | – | 50 | 0 | 8 |
| October 14 | 17 | – | Not recorded | 0 | 8 |
| October 15 | 18 | – | 38 | 0 | 8 |
| October 16 | 19 | – | 7 | 0 | 8 |
| October 17 | 20 | – | 8 | 0 | 8 |
| October 18 | 21 | – | 1.6 | 0 | 8 |
| October 19 | 22 | – | 7.5 | 0 | 8 |
| October 20 | 23 | – | 7 | 0 | |
| October 21 | 24 | – | 1 | 0 | |
| October 22 | 25 | – | 0 | 0 | |
| October 23 | 26 | – | 0 | 0 | |

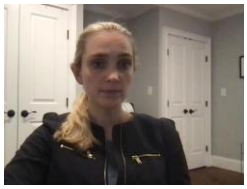
*Data for 16 hours.



9

# Case description: Buprenorphine taper

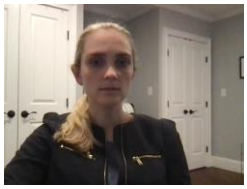
- Day 25: Patient requested to be tapered off opioids prior to discharge
  - Stopped morphine PCA on day 25
  - Elected for rapid taper of buprenorphine
    - Tapered off in 2 days (day 27)
  - No symptoms of opioid withdrawal



10

# Discussion

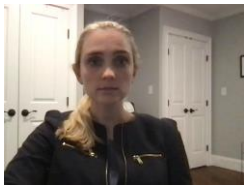
- Sublingual buprenorphine as alternative to IV opioids
  - Typical course after surgery is short course of IV analgesics → oral analgesics
  - Not all patients can tolerate PO medications
    - Alternatives to PO
      - Rectal (sometimes contraindicated in GI surgery)
      - Transdermal fentanyl (slow onset)
      - Buccal fentanyl (cost, insurance coverage as outpatient)
      - Sublingual buprenorphine
        - Rapid systemic availability
        - 24-60 hour half-life



11

# Discussion

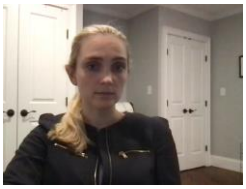
- Concurrent use of buprenorphine and opioid antagonists
  - Concern regarding buprenorphine partial μ-opioid antagonism
  - However, preclinical data: interaction between buprenorphine and full opioid agonists (FOA) is **dose dependent** (Kögel 2005)
    - **Moderate** buprenorphine dose + FOA -> **full efficacy** of FOA
    - **High** buprenorphine dose + FOA -> **antagonism** of FOA



12

# Discussion

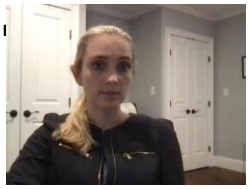
- Concurrent use of buprenorphine and opioid antagonists
  - Clinical data: supports synergistic/additive effect of buprenorphine + FOA
    - Combination effective at controlling **cancer pain** (Mercadante 2006, Beltrutti 2000), **perioperative analgesia** (Beltrutti 2002)
    - Patients on FOA can be switched to buccal buprenorphine at **50% FOA** without need for FOA taper or with risk of withdrawal (Webster 2016)
    - Synergistic/additive effect achieved at dose range of **8-12 mg** buprenorphine daily (Greenwald 2007, Greenwald 2014)
      - Perioperative guidelines recommend continuing buprenorphine at 8-12mg daily throughout perioperative period (Quaye 2019, Lembke 2019, Warner 2020, Quaye 2020)



13

# Discussion

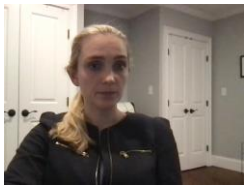
- Dosing schedule for initiating buprenorphine in literature
  - Microdoses for induction with concurrent FOA use: Bernese method
    - Eliminates need for patients to abstain from FOAs and experience withdrawal symptoms before initiating buprenorphine
  - Prior reports
    - In patients with history of OUD
      - Start at 0.2 mg sublingual buprenorphine daily, increase to 12 mg daily over 9 days or 24 mg daily over 28 days (Hämmig 2016)
      - Start at 0.5 mg, increase to 12 mg daily over 8 days (Terasaki 2019)
    - In perioperative setting
      - **Assumption is that patients who do not have OUD may tolerate a more rapid i protocol**
      - Start at 2 mg daily, increase to 12 mg daily over 5 days (Lee 2020)



14

# Discussion

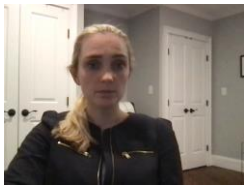
- Dosing schedule for our patient
  - Started on daily buprenorphine dose of **1 mg** (0.5mg BID) - in addition to transdermal fentanyl patch + PO opioid + IV opioid
    - Prior to starting microdosing, she required > 80mg IV morphine daily
    - After starting buprenorphine, steady decrease in IV morphine use



15

# Conclusion

- Presented case of patient requiring high dose IV opioids who was unable to use oral agents. Successfully transitioned to sublingual buprenorphine with rapid microdosing induction course
- Concurrent use of buprenorphine and FOA for acute pain treatment is feasible
- Buprenorphine can be used to transition patients off of FOA
  - Especially useful in patients with gastrointestinal symptoms/contraindications who cannot take oral FOA



16