Inpatient Buprenorphine Use for Pain Management

James J. Brehany, MD
Assistant Professor
Department of Internal Medicine
Division of Palliative Medicine
The Ohio State University Wexner Medical Center

MedNet21
Center for Continuing Medical Education

The Ohio State University Wexner Medical Center

Objectives

- **Describe** the properties of buprenorphine that make it a safe and effective analgesic medication for the hospitalized patient
- For cancer and non-cancer populations:
  - **Identify** appropriate groups for buprenorphine-based analgesia
  - **Show** how to initiate and utilize buprenorphine-based analgesic therapy in the hospital
- **Discuss** the challenges of using buprenorphine in the hospital

What This Presentation Is *NOT*

- Perioperative Management
- Micro-dosing
- Pain management for patients with opioid use disorder (OUD)

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- Perioperative Management
- Micro-dosing
- **Pain management for patients with opioid use disorder (OUD)**

Common Misconceptions

- Patients taking buprenorphine must have a history of an OUD
- "Regular" opioids won't be effective for patients taking buprenorphine products
- Buprenorphine does not provide the same analgesic benefits as full agonist opioids
- Patients will withdraw if given buprenorphine in addition to full agonist opioids

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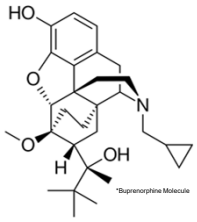
Definitions and Pharmacology

Opioid Receptor Types

- Mu
- Kappa
- Delta



*Buprenorphine Molecule

Definitions and Pharmacology

Opioid Receptor Binding

	Mu	**Delta**	**Kappa**
Morphine	Fully Agonizes	Fully Agonizes	Fully Agonizes
Buprenorphine	Partially Agonizes	Antagonizes	Inversely Agonizes

Definitions and Pharmacology

Partial Agonism

- Partial Agonist ≠ Weaker Opioid
- Increased Binding Affinity

Buprenorphine Products

Delivery Methods ("Brand Name")

- Transdermal Patch ("Butrans")
- Intravenous Injection ("Buprenex")
- Buccal Film ("Belbuca")
- Sublingual Tablet ("Subutex")
- Sublingual Film ("Suboxone" / "Zubsolv")
- Long-acting Intramuscular Injection ("Sublocade")

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Buprenorphine Products

Available Dosages and Daily OME Potencies

	Dosages	OME
Transdermal Patches	5, 7.5, 10, 15, 20 mcg/hour	~12 – 48 OME/day
Intravenous	0.1 mL = 0.03 mg	~9 – 90 OME/dose
Buccal Films	75, 150, 300, 450, 600, 750, 900 mcg films	~15 – 90 OME/day
Sublingual Films / Tablets	1, 2, 4, 8 mg films / tabs	~60 – 480 OME/day

Key:
OME: "Oral Morphine Equivalent"
Mg: "Milligram"
Mcg: "Microgram"

Buprenorphine Products
Bioavailability and Conversions

	Bioavailability	Rough Conversion
Transdermal Patches	~15%	See Upcoming Slide
Intravenous	100%	0.01 mg / 10 mcg ≈ 1 OME
Buccal Films	~50%	0.15 mg / 150 mcg ≈ 7.5 OME
Sublingual Films / Tablets	~30%	1 mg / 1000 mcg ≈ 30 OME

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Buprenorphine Products
Reference Chart

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Buprenorphine Products
5mcg/hour Transdermal "Butrans" patch

$$\frac{5\ mcg}{1\ \text{hour}} x\ \frac{24\ \text{hours}}{1\ \text{day}} x\ \frac{1\ \text{mg}}{1000\ mcg} x\ \frac{\sim 1\ \text{OME}}{0.01\ \text{mg}} = \sim \mathbf{12}\ \text{OME/day}$$

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Buprenorphine Products
Benefits of Transdermal Buprenorphine

- Opioid sensitive patients who require a long acting:

Modality	Potency
Fentanyl TD Patches	30 OME/day
MS Extended Release	30 OME/day
Oxycodone Extended Release	30 OME/day

Modality	Potency
Butrans 5 mcg/hour TD patch	12 OME/day
Butrans 7.5 mcg/hour TD patch	18 OME/day
Butrans 10 mcg/hour TD patch	24 OME/day

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Buprenorphine Products
Benefits of Transdermal Buprenorphine

- Patients who struggle with complex medication regimens:

Modality	Duration
Fentanyl TD Patches	q72 hours
MS Extended Release	BID-TID
Oxycodone Extended Release	BID-TID

Modality	Duration
Butrans 5 mcg/hour TD patch	q7 days
Butrans 7.5 mcg/hour TD patch	q7 days
Butrans 10 mcg/hour TD patch	q7 days
Butrans 15 mcg/hour TD patch	q7 days
Butrans 20 mcg/hour TD patch	q7 days

Key:
BID: Twice Daily
TID: Three Times Daily

Buprenorphine Products
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Set it and forget it

Buprenorphine Products
Benefits of IV Buprenorphine

- Extended duration of action

	IV Fentanyl	IV Hydromorphone	IV Buprenorphine
Onset of Action	~1.5 mins	< 5 mins	~5-15 mins
Time to Peak Effect	~5-15 mins	~10-20 mins	~1 hour
Plasma Half-Life	~2.5 hours	~4 hours	~2-7 hours
Duration of Action	~60 mins	4-5 hours	6-8 hours

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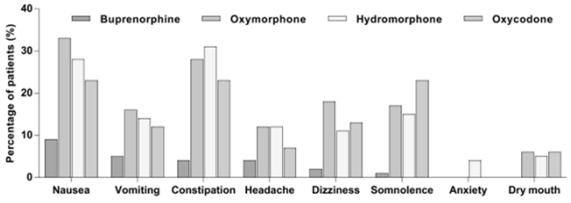
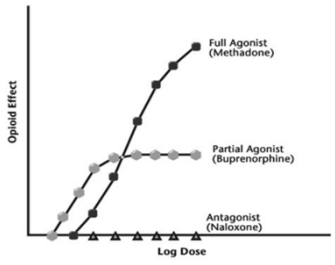
Buprenorphine Products
Unique Properties of Buprenorphine



Buprenorphine Products
Unique Properties Of Buprenorphine

- Decreased risk for sedation / cognitive dysfunction
- Decreased risk for constipation
- Possible benefit for neuropathic pain
- Lack of euphoria
- Respiratory ceiling effect

Buprenorphine Products
Respiratory Ceiling Effect



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Director, Pulmonary-Palliative Clinic
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Identification of Appropriate Population

Who are the patients who can benefit from buprenorphine?

?

Identification of Appropriate Population

Who are the patients who can benefit from buprenorphine?

(Almost)

EVERYONE

Identification of Appropriate Population

- Acute pain/ Post-operative pain
- Chronic Pain Syndrome
- Special Population Consideration
  - ESRD
  - Liver Disease
  - Heart Failure
  - Acute Critical Illness
  - Chronic Lung Disease
  - Geriatric Population
- Cancer-related pain

Identification of Appropriate Population

Acute Pain Management

- Systematic Review, 28 studies included (n= 2200)
- Population: ED, acute MI, acute fracture, surgical
- Methods: Compared buprenorphine to morphine
- Results:
  - No difference in pain
  - No difference in incidence of respiratory depression
  - No difference in sedation
  - Less pruritus
- **Takeaway**: Buprenorphine is as effective with less side effects

Identification of Appropriate Population

Acute Pain in Post-Operative Patients

- Prospective Randomized Trial
  - 200 patients
- Surgery: Total Knee Replacement
- Methods: Transdermal Patch applied at end of surgery
- Results:
  - Pain scores at rest ↓↓ (P = 0.0083)
  - Pain scores with movement ↓↓ (P = .012)
  - Satisfaction scores much higher
  - Adverse effects lower (especially PONV)
- **Takeaway**: Improved pain control and less side effects

Identification of Appropriate Population

Acute Pain in Pediatric Patients

- Systematic Review, 4 studies n= 195 patients
- Methods: Comparing IV buprenorphine to IV morphine; post-surgical patients
- Results:
  - Time to breakthrough analgesia significantly longer in buprenorphine group (114 min)
  - No significant difference in respiratory depression
  - No significant difference in SE (nausea, sedation, pruritus)
- **Takeaway**: Improved pain control with no difference in side effects

Identification of Appropriate Population

Chronic Pain Management

- OA (Hip/knee)
  - Moderate severity
  - Non-inferior to tramadol, codeine/acetaminophen
- Low Back Pain
  - Moderate severity
  - Significantly more effective than placebo
- Side effects
  - In active-comparator trials broadly similar to alternatives used

Takeaway: Multiple studies support analgesic efficacy of TD buprenorphine for chronic pain

Identification of Appropriate Population

Treatment of Chronic Pain in Veterans

VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE USE OF OPIOIDS IN THE MANAGEMENT OF CHRONIC PAIN

Department of Veterans Affairs
Department of Defense

Recommendation

5. For patients receiving daily opioids for the treatment of chronic pain, we suggest the use of buprenorphine instead of full agonist opioids due to lower risk of overdose and misuse. **(Weak for | Reviewed, New-added)**

Identification of Appropriate Population

Special Population Considerations

ESRD
- No dose adjustment

Liver Disease
- No dose adjustment in mild-moderate impairment

Heart Failure
- Lower risk for QTc prolongation

Geriatric Population
- No need for dose adjustments
- Ease of administration
- Lower rate of drug-drug interactions

Chronic Lung Disease
- Respiratory ceiling effect
- Dyspnea

Acute Critical Illness
- Tenuous respiratory status
- Organ failures
- Current research underway

Identification of Appropriate Population

Cancer Patients

What about **cancer-related pain** and **buprenorphine**?

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Identification of Appropriate Population

Long-term management of cancer-related pain

- Corli et al in 2016 led an RCT with intention to treat protocol comparing oxycodone, oral morphine, TD fentanyl, and TD buprenorphine for 28 days in patients with cancer-related pain
  - 498 patients across four hospital systems
- No significant difference between the four agents and analgesic responses
- When compared with buprenorphine:
  - PO Morphine required more frequent rotation to alternative agents
  - TD Fentanyl required more frequent dose titration
- **Takeaway**: Buprenorphine is an effective and stable backbone for analgesic regimens

Identification of Appropriate Population

Rotation to alternative agents

- Aurilio et al in 2009 explored impact of rotating to alternative, lower dose, transdermal opioids
  - Small study (32 patients)
  - Half started on TD fentanyl before rotation to TD buprenorphine
  - Other half started on TD buprenorphine before rotation to TD fentanyl
- No significant difference in pain or rescue medication requirements between groups despite the 50% dose decrease
- **Takeaway**: Full agonist regimen is not an absolute barrier to TD buprenorphine rotation

Identification of Appropriate Population

Is buprenorphine ready for primetime in cancer patients?

- American Journal of Hospice and Palliative Medicine, 2014
  - Article by Eric Prommer: **Yes**
    - Excellent safety profile
    - Neuropathic benefit
    - Increasing ease of conversion
- Cochrane Review, 2015
  - Article by Schmidt-Hansen: **Less clear**
    - No great evidence to recommend
    - Conclusion based very low-quality studies

Identification of Appropriate Population

Societal Recommendations

- European Society of Medical Oncologists
  - **Yes** – for cancer patients with renal dysfunction
- National Institute for Health and Clinical Excellence (United Kingdom)
  - No significant difference in efficacy between morphine, oxycodone, TD fentanyl, and TD Buprenorphine

Identification of Appropriate Population

Societal Recommendations

- National Comprehensive Cancer Network:

  "Buprenorphine is increasingly recognized as an effective analgesic with an improved therapeutic index relative to certain potent opioids, however, it has not been extensively studied in cancer pain. Its use in cancer pain is extrapolated from data on its effectiveness in non-malignant chronic pain."

Identification of Appropriate Population

Societal Recommendations

- National Comprehensive Cancer Network:

  "Although RCT data on buprenorphine for treating cancer pain are somewhat limited, several case series, prospective uncontrolled studies, and a few randomized trials support it's use in cancer-related pain."

Identification of Appropriate Population

…More research is needed

Identification of Appropriate Population
General Benefits of Buprenorphine

- Decreased euphoric effects
- Decreased risk for constipation
- Some neuropathic benefit compared to other opioids

Identification of Appropriate Population
Inpatient Benefits of Buprenorphine

- Ceiling effect on respiratory suppression
- Decreased risk for sedation
- Multiple delivery methods (including IV)

Identification of Appropriate Population
Appropriate Patients

- Sensitive to full-agonist opioids
- In need of low-dose long-acting agents
- A history of respiratory/renal comorbidities
- In need of a longer-acting IV agent

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Utilization of Buprenorphine in the Hospital

Cancer Patient

- 45 y/o M w/ PMH relevant for newly diagnosed NSCLC who is admitted for uncontrolled back pain. At baseline, he takes no medications and states that he is hesitant to use opioid medications as his brother overdosed on fentanyl many years ago. Scans show progressive metastatic lesions throughout the thoracic spine. An EKG demonstrates a qtc of 540. You are consulted for assistance with pain management.
  - Think about how you would approach this case before today…
  - Think about how you would approach this case with buprenorphine…

Utilization of Buprenorphine in the Hospital

Cancer Patient

- How I would think about it:
  - IV Buprenorphine
    - Start 0.09 – 0.15mg q4h PRN for dose finding
      - This gives access to up to 90 OME in 24-hour period
  - TD Buprenorphine
    - Assess 24-hour opioid requirements and start 50-75% of total requirements as patch
      - Continue IV option as patch can take up to 3 days to reach full effect
      - Send script to pharmacy ASAP to ensure stock and prior authorization are addressed
  - Optimization of adjuvant agents
    - Steroids
    - Radiation Oncology consult
    - Topical agents (Lidocaine Patches, Voltaren, Heat)

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Utilization of Buprenorphine in the Hospital

Acutely Critically Ill Patient

- 77 y/o F w/ a PMH of osteoarthritis, COPD, DM2, and CKD3 is admitted for hip replacement. Her hospital course was complicated by hypoxic resp failure requiring intubation and AKI on CKD. She's now extubated to high flow nasal canula and has become severely debilitated. She has not been able to work with PT due to pain despite scheduled APAP and PRN oxycodone 5-10mg q4h PRN which she has not been taking. You are consulted for assistance with symptom management.
  - Think about how you would approach this case…

Utilization of Buprenorphine in the Hospital

Acutely Critically Ill Patient

- How I would think about it:
  - What I DON'T want to use:
    - Oxycodone- Pt not comfortable / too sedating
    - Morphine – renal disease
    - NSAIDs- renal disease
  - IV Buprenorphine
    - Start 0.09 q6h PRN, but instruct her that we can go up from here
    - This gives access to up to 36 OME in 24-hour period
  - Optimization of adjuvant agents
    - Continue acetaminophen
    - Ice/heat as indicated
    - Lidocaine patch

Utilization of Buprenorphine in the Hospital

Heart Failure Patient

- 45 y/o M w/ a PMH of familial cardiomyopathy s/p LVAD placement in 2021 and QTc prolongation. Admitted for heart failure exacerbation and reports increasing pain despite regimen of gabapentin 600mg TID and oxycodone 5mg q4h PRN (averaging ~5 tabs/day). Endorses need for overnight PRNs and lack of sleep is impacting quality of life. Hospital course has been complicated by severe constipation. You are consulted for assistance with pain management.
  - Think about how you would approach this case…

Utilization of Buprenorphine in the Hospital

Heart Failure Patient

- How I would think about it:
  - His oxycodone is effective at controlling pain but burdens of frequent administration and side effect of constipation resulting in poorer QOL
  - Using approx. 37.5 OME per day
  - Option 1: TD Buprenorphine + oxycodone prns
    - Start 50%-75% total requirements as a patch
      - Start Buprenorphine patch 10mcg/hr
    - Continue PO oxycodone 5mg q4h prn
  - Option 2: TD Buprenorphine as single agent
    - Fold 100% of OME requirement into patch
      - Start with Buprenorphine patch 10mcg/hr + continue prn oxycodone
      - Re-eval OME on day 3 and consider up-titration to 15mcg/hr or appropriate dose
    - Acetaminophen prn
  - Evaluate outpatient provider options and need for PA

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Challenges of Using Buprenorphine

Seems like we should be using more buprenorphine products in the hospital…

Let's check in and see how its going!

Challenges of Using Buprenorphine

Provider Concerns

- "I've seen it used in acute pain but I never use it unless palliative tells me to"
- "I never use it on my own, I want more information on it though"
- "I don't know the dosing"
- "Super helpful" (but I don't order it unless palliative tells me to)

Challenges of Using Buprenorphine

Bedside RN Concerns

- "I don't use it that often but it worked well when I did"
- "I used [sublingual buprenorphine] on a vented patient once…they told me just to do it but I didn't know if I was doing it right"
- "It's easy in tubed patients"
- "I don't know the dose I am giving"

Challenges of Using Buprenorphine

Colleague Feedback

- This is what I am **NOT** hearing:
  - It is ineffective
  - My patients could not tolerate
  - I don't like to use this medication
- This is what I am hearing:
  - It can be effective in treating patient's pain, but we ALL need more education on it

Challenges of Using Buprenorphine
Where do we go from here?

- **Staff Education** is critical to obtain buy-in and improve comfort with administration
  - Faculty, APPs, Trainees, Bedside RNs
  - "Not an opioid blocker"
- **Patient education** is critical to obtain buy-in and reduce stigma
  - Why are we using this? Because it is a *great* analgesic medication
- **Prior Authorization** may need to be obtained
  - Generally successful when we explain our reasoning
- **Inpatient to Outpatient Transition**
  - Needs to be considered especially when initiating long-acting agent
  - With education we have had success with various providers including PCPs taking on these scripts

Challenges of Using Buprenorphine
Less Appropriate Inpatients

- Individuals receiving >200 OME/day
  - Entering the realm of microdosing
- Rapidly escalating pain needs
  - Would methadone be a better fit?
- Uninsured patients
  - Transdermal buprenorphine products are unfortunately very expensive

Challenges of Using Buprenorphine
We Hope You're Not Feeling Like This…

Conclusions

- Buprenorphine has a favorable side effect profile which makes it a GREAT choice for treating pain in some of our medically fragile hospitalized patients with multiple comorbidities
- Buprenorphine is an effective agent for treating various types of pain outside the context of opioid use disorder
- The diversity of available formulations allows buprenorphine to be a part of numerous analgesic regimens
- A major challenge of incorporating buprenorphine into more widespread practice is lack of familiarity across the healthcare field (with education, we can change this!)

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Conclusions

If We Didn't Convince You, Maybe Chat GPT will…

Buprenorphine, oh how you soothe
Pain and discomfort, you help us move
With your power to block those receptors
You ease our suffering, you're a lifesaver
Unlike opioids that cause addiction
You're less likely to lead to affliction

Your ceiling effect keeps us safe
From respiratory depression, a deadly race
You can be used for acute or chronic pain
From surgery to cancer, you never wane
You come in many forms, a patch or a pill
Or a sublingual film, that dissolves with a thrill

Buprenorphine, you're a game changer
A medicine that we can't ignore or danger
Your benefits are vast, your side effects few
We thank you for all you can do

Thank You!

- The OSU Palliative Pharmacist Group
  - Justin Kullgren
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  - Jessica Hirsch
  - Maureen Saphire
- The MICU Pharmacist Group
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- Jillian Gustin

Bibliography

All references are available in slide deck notes