Clinical Pearls in Palliative Medicine
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• No financial disclosure

• I will be discussing the off label use of methylphenidate, naltrexone, rifampin, sertraline, dronabinol, gabapentin, metoclopramide, baclofen, olanzapine
Case 1
A 76 y.o. woman with severe long standing joint destructive rheumatoid arthritis presents to your clinic for follow up of her chronic constipation. She continues to report ongoing symptomatic constipation unrelieved by her current regimen requiring enemas several times a week. Medical work-up of her constipation has been unrevealing. Her pain is currently well controlled on her current opioid regimen and improved pain control has allowed her to achieve independence in her ADLs.

Current medications include:

- Prednisone 10mg daily
- Extended-release morphine 60mg bid
- Senna 4 tablets bid
- Polyethylene glycol 17gm in 8oz liquid bid
- Bisacodyl 3 tab tid
Which of the following interventions would be the next best step in managing her constipation?

A. Switch her from oral morphine to a fentanyl patch  
B. Add methylnaltrexone 12mg subQ injection daily to the current laxative regimen  
C. Add lactulose 30mL po qid prn  
D. Stop laxative regimen and begin naloxegol 25mg po daily  
E. Discontinue opioid pain medications
Answer

D. Stop laxative regimen and begin naloxegol 25mg po daily
Opioid Induced Constipation

A. Switch her from oral morphine to a fentanyl patch

B. Add methylnaltrexone 12mg subQ injection daily to the current laxative regimen

C. Add lactulose 30mL po qid prn

D. Stop laxative regimen and begin naloxegol 25mg po daily

E. Discontinue opioid pain medications

• No opioid is better than another*
Opioid Induced Constipation

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E. Discontinue opioid pain medications

• Already on an aggressive laxative regimen.
Opioid Induced Constipation

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D. Stop laxative regimen and begin naloxegol 25mg po daily

E. Discontinue opioid pain medications • Improve constipation at the expense of pain control
Opioid Induced Constipation

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C. Add lactulose 30mL po qid prn

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E. Discontinue opioid pain medications

• Stop laxative regimen when starting PAMORA
Peripheral Acting Mu-Opioid Receptor Antagonists (PAMORAs)

- Do not cross the blood brain barrier
- Block mu receptors in the gut but NOT the CNS
- Indicated for opioid induced constipation that fails to respond to aggressive laxative regimen
- Bowel obstruction absolute contraindication
- Stop laxatives at initiation --- can add back on day 3 if response to PAMORA inadequate


# Methylnaltrexone vs. Naloxegol

<table>
<thead>
<tr>
<th></th>
<th>Oral Methylnaltrexone</th>
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<th>Naloxegol</th>
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<tr>
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<td>non-cancer pain</td>
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<td></td>
<td>Hepatic failure</td>
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<tr>
<td><strong>COST</strong></td>
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<td><strong>RISK</strong></td>
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<td>Bowel perforation in bowel wall that lacks integrity*</td>
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</table>
Chronic opioids > 4 weeks
Failed laxative regimen
No bowel obstruction

Advanced illness

SubQ methylnaltrexone

Non-cancer pain

Hepatic failure
CYP3A4 inhibitor

Naloxegol or Oral methylnaltrexone

Oral methylnaltrexone
Clinical Pearl

Consider oral peripheral acting mu-opioid receptor antagonists (PAMORAs) in outpatients with opioid induced constipation who have failed aggressive laxative regimen.
Case 2
A mildly anxious, never married, 79 y.o. woman is on your clinic schedule as a hospital follow up after her 4th hospitalization in the last 9 months. She has multiple medical co-morbidities and has been clinically and functionally declining over the last year. You recognize her life expectancy at less than 1 year and further recognize the need to do some advance care planning but worry about how this patient might respond to a conversation about what the future may hold for her.
Which of the following statements about advance care planning for this patient with a serious illness is true?

A. Advance care planning does not worsen anxiety, depression or hopelessness

B. Patients with serious illness will bring up advance care planning topics themselves when they are ready to discuss them.

C. Advance care planning is ideally done when there is a therapeutic decision that needs to be made.

D. While it decreases non-beneficial care at the end-of-life, it has no impact on patient quality-of-life or family bereavement.

E. Physician Order for Life Sustaining Treatment (POLST) form is synonymous with advance care planning.
Answer

A. Advance care planning does not worsen anxiety, depression or hopelessness
Terminology

Advance Care Planning

Serious Illness Conversation

Goals of Care

Diagnosis

Prognosis <1 year

Crisis
Answers

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• Numerous studies show improved QoL after ACP
• Several studies suggest ACP alleviates anxiety
• Improved depressions scores after palliative medicine consultations
• At a minimum these conversations do not harm patients or families

Answers

A. Advance care planning does not worsen anxiety, depression or hopelessness.

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- Patients expect their physician to initiate the conversation.

Answers

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• Crisis decision making is never ideal

Answers

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E. Physician Order for Life Sustaining Treatment (POLST) form is synonymous with advance care planning.

- less non-beneficial care at the end-of-life
- care congruent with wishes
- improved quality of life for the patient
- improved family bereavement
- reduced overall cost of care

Answers

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C. Advance care planning is ideally done when there is a therapeutic decision that needs to be made.

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E. Physician Order for Life Sustaining Treatment (POLST) form is synonymous with advance care planning.

- POLST is a physician order
- A signed POLST \textit{presumes} a serious illness conversation has occurred.
- All POLST should be tied to a documented conversation explaining the \textit{rationale} for the decisions made in the POLST
- POLST without conversation is dangerous
Clinical Pearl

Serious illness conversations/advance care planning does not worsen anxiety.
Clinical Pearl

Serious illness conversations/advance care planning does not worsen anxiety.

BONUS PEARL

Documented Conversation → POLST
Case 3
A 38 y.o. woman with metastatic breast cancer is admitted to your hospital service with dehydration secondary to nausea and vomiting for the last 36 hours. The onset of her nausea coincides with the initiation of morphine for cancer related pain. There have been no other recent medication changes and she has tolerated her stable chemotherapy regimen without nausea. She had a normal BM this morning.
Which intervention is most appropriate to manage her opioid induced nausea?

A. Switch opioids from morphine to fentanyl for pain
B. Continue morphine and add scheduled prochlorperazine for 5 days
C. Stop morphine and start a lidocaine patch
D. Continue morphine and add ondansetron as needed
E. Switch from morphine to tramadol pain
B. Continue morphine and add scheduled prochlorperazine for 5-7 days
Principles of Opioid Induced Nausea Management

• Occurs occasionally --- 15-40% of patients

• Tolerance develops in >90% in 3-7 days

• Little evidence to support one opioid over another*
  • **Avoid opioid rotation in the first 5 days**
Vomiting

Cortex / Emotional Stimuli

Vestibular Center

Chemoreceptor Trigger Zone

Gastric Irritation/Distention

Intracranial Pressure Receptors

Vomiting Center

Vomiting
Vomiting

Cortex / Emotional Stimuli

Vestibular Center

Gastric Irritation / Distention

Chemoreceptor Trigger Zone

• Metabolic Derangements
• Drugs, Toxins

Intracranial Pressure Receptors

Vomiting
Vomiting

Vomiting Center

- Cortex / Emotional Stimuli
- Vestibular Center
- Gastric Irritation/ Distention
- Chemoreceptor Trigger Zone
  - 5HT-3 Antagonists
  - Corticosteroids
  - Dopamine Antagonists
  - NK-1 inhibitors
- Intracranial Pressure Receptors

5HT-3 Antagonists
Corticosteroids
Dopamine Antagonists
NK-1 inhibitors
Principles of Opioid Induced Nausea Management

• Multiple mechanisms
  • vestibular, gut inertia, CTZ
  • Anti-dopaminergic agents first line in opioid induced N/V

• Schedule anti-emetics to ‘treat through’

Clinical Pearl

• Anti-dopaminergic antiemetics are first line therapy for opioid induced nausea.
Case 4
A 48 y.o. woman presents to your office for routine follow up her primary biliary cirrhosis. She complains of relentless, severe pruritus that prevents her from sleeping. She is desperate for relief. She has failed prior trials of all topical agents, as well as diphenhydramine, doxepin, loratadine and hydroxyzine. She is already taking high dose cholestyramine.

Her PMH is significant for a remote history of IV heroin use now on methadone maintenance therapy. She is HIV positive with an undetectable viral load, well managed on HAART. MEDS: cholestyramine 4gm bid, methadone 20mg daily, Atazanavir 300 mg/ritonavir 100 daily. She has widespread excoriations on exam.
Which of the following interventions is most appropriate to manage her cholestatic pruritus?

A. Naltrexone 12.5mg po bid
B. Rifampin 150mg po tid
C. Sertraline 100mg po daily
D. Dronabinol 10mg po tid
E. Gabapentin 600mg po tid
C. Sertraline 100mg po daily
Answer

- Naltrexone 12.5mg po bid
- Rifampin 150mg po tid
- Sertraline 100mg po daily
- Dronabinol 10mg po tid
- Gabapentin 600mg po tid

Effective but reverses opioids leading to opioid withdrawal

Answer

- Naltrexone 12.5mg po bid
- Rifampin 150mg po tid
- Sertraline 100mg po daily
- Dronabinol 10mg po tid
- Gabapentin 600mg po tid

- Effective but multiple drug interactions


Answer

• Naltrexone 12.5mg po bid
• Rifampin 150mg po tid
• Sertraline 100mg po daily
• Dronabinol 10mg po tid
• Gabapentin 600mg po tid

• Paucity of evidence.

Answer

- Naltrexone 12.5mg po bid
- Rifampin 150mg po tid
- Sertraline 100mg po daily
- Dronabinol 10mg po tid
- Gabapentin 600mg po tid

• Effective in uremic pruritus. Never studied in cholestasis.


Answer

- Naltrexone 12.5mg po bid
- Rifampin 150mg po tid
- Sertraline 100mg po daily
- Dronabinol 10mg po tid
- Gabapentin 600mg po tid

‘Best’ evidence.


Clinical Pearl

- Naloxone/Naltrexone, Sertraline and Rifampin are effective agents for cholestatic pruritus.
Case 5
A 57 y.o. Amish man with a history of longstanding dyspepsia managed with sodium bicarbonate slurry is admitted to your hospital service with persistent hiccups for the last 48 hours to the point of being unable to maintain sleep or hydration. EGD reveals only evidence of GERD. In addition to antireflux therapy, you start him on chlorpromazine 25mg IV q6h escalating the dose to 50mg IV q6h without benefit to his hiccups.
Which of the following is a reasonable second line therapy for the management of this patient’s hiccups?

A. Amlodipine  
B. Baclofen  
C. Lorazepam  
D. Phrenic nerve ablation  
E. Dexamethasone
Answer

B. Baclofen
Hiccups
Hiccups

FDA Approved

• Chlorpromazine (case series)

Evidence for benefit

• Metoclopramide* (RDBPCT)
• Baclofen (prospective cohort)
• Gabapentin (case series)
Hiccups

A. Amlodipine
B. Baclofen
C. Lorazepam
D. Phrenic nerve ablation
E. Dexamethasone

Hiccups

A. Amlodipine
B. Baclofen
C. Lorazepam
D. Phrenic nerve ablation • Last resort
E. Dexamethasone

Clinical Pearl

• Metoclopramide and baclofen are considered second line agents in the treatment of hiccups.
Case 6
A 74 y.o. woman is admitted to your hospital service with severe GOLD stage IV COPD and dyspnea. She is on maximal medical management for her COPD. Her oxygen saturation is 94% on 2L nasal cannula at rest and with activity. Her main symptom is severe breathlessness with minimal exertion. She is functionally independent in all her ADLs. Her goal is to maximize her quality of life. She reports intolerances to multiple oral medications (including delirium from multiple opioids) and strongly desires to avoid oral medications if at all possible.
Which of the following interventions is most likely to improve her dyspnea?

A. Morphine 2.5mg nebulized qid
B. Use a fan for as needed for dyspnea relief
C. Prescribe a gait aid such as a walker to help relieve her dyspnea
D. Increase her oxygen to 4L nasal cannula
E. Prescribe ABH (Ativan-Benzodrexil-Haldol) gel massaged into the inner wrist three times a day for dyspnea
C. Prescribe a gait aid such as a walker to help relieve her dyspnea.
Dyspnea
Dyspnea

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Ekström M, Abernethy AA, Currow DC. The management of chronic breathlessness in patients with advanced and terminal illness. *BMJ* 2015;349:g7617

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Non-pharmacologic Dyspnea Management

• No evidence for or against fans
• Moderate evidence for gait aids
• Strong evidence for chest wall vibration and neuromuscular stimulation

Ekström M, Abernethy AA, Currow DC. The management of chronic breathlessness in patients with advanced and terminal illness. BMJ 2015;349:g7617

Clinical Pearl

• Gait aids are simple, widely available and effective for dyspnea management in patients with COPD.