Applying Quality to Postsurgical Opioid-Induced Constipation

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Faculty and Staff Disclosures

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Ernest J. Dole, PharmD, PhC, FASHP, BCPS, has no relevant financial relationships with commercial interests to disclose.

Pharmacy Times Continuing Education™ Planning Staff: Dave Heckard; Maryjo Dixon, RPh; Dipti Desai, PharmD, RPh; Jyoti Arya, PharmD, RPh; Susan Pordon; and Donna Fausak have no financial relationships with commercial interests to disclose.

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Learning Objectives

At the completion of this activity, participants will be able to:

• Demonstrate an understanding of the prevalence and severity of OIC caused by postsurgical opioid prescribing
• Examine current and emerging pharmacologic treatments that can be used to prevent and treat OIC
• Determine quality metrics that should be monitored to ensure that patients receive safe and effective opioid treatment
• Identify the role of pharmacists in the prevention and treatment of OIC

Use of Opioids in Chronic Pain: Balancing Act

Pain as the 5th vital sign

Starting in 2001, the Joint Commission officially recognized that pain is a major health problem and that “patients have the right to appropriate assessment and management of pain.”

A Balancing Act: Public Health

A crisis of abuse of prescription opioid medication


Among 47,055 drug overdose deaths that occurred in 2014 in the United States, 28,647 (60.9%) involved an opioid.

A Balancing Act: Patient’s Expectations

- Of being pain free
- Of “magic bullet” medications
- Of presence of undesirable and unexpected adverse effects of opioids (i.e., constipation)
- Of unlimited supply of medications
  - opioids while being prescribed chronic opioid therapy (COT) for chronic noncancer pain (CNCP)
  - of not having to do any work
  - Of physical therapy
  - Of behavioral health
  - Of no consequences for their decisions
  - Of “being honest”

A Balancing Act: Providers’ Realities

- The incidence of alcoholism and addiction in the general population is 5%-10%
- One addict affects 7-10 people
- The prevalence of current or past substance use disorders in patients receiving chronic opioids for CNCP may be ~ 40% or higher
- The principles of chronic medication management are often forgotten when managing opiate medication
  - Clash of providers’ and patients’ values

Classification and Identification of OIC

- The Rome III criteria definition of constipation is generally used to identify OIC although there is no consistent definition.
- Consensus definition has been developed to standardize future clinical trials:
  - Change from baseline in bowel habits and change in defecation patterns after the initiation of opioid therapy
  - Patterns are characterized by the occurrence of the following: decreased frequency of spontaneous bowel movements (BM), worsening of straining to pass BMs, sense of incomplete evacuation, or harder stool consistency

Prevalence of Opioid-Induced Constipation (OIC) in Opioid Management

- Prescribing rates of opioids are approximately 37%-50% in postoperative surgery setting
- OIC is the most common gastrointestinal adverse effect impacting patients who take opioids
  - A meta-analysis reveals that the prevalence of OIC in noncancer patients receiving opioids is 41%; however, this rate varies from 14% to 90% in individual studies
  - The likelihood of OIC increases as the duration of opioid use increases, and patients may discontinue opioid therapy upon the development of constipation
### Complications of Untreated/Mismanaged OIC

- Patients may be at increased risk for bowel dysfunction, fecal impaction, incontinence, and inadequate drug absorption.
- Studies illustrate that work productivity and activity impairment decreases due to this condition, equaling to approximately 14 hours of lost productivity per week.
- Patients are more likely to alter their dosing regimen due to this adverse effect; 28% of patients use lower doses; 33% of patients will skip, decrease, or eliminate doses to ease constipation.
- Ripple out effect of these decisions on therapy.


### Impact of OIC

Prospective, longitudinal, observational cohort study conducted in the United States, Canada, Germany, and the United Kingdom in patients aged 18-85 years (N = 489), who had been receiving daily opioid therapy for ≥4 weeks for chronic noncancer pain with presence of OIC in the past 2 weeks:

- Importance and severity of OIC are perceived differently by patients and their providers.
- This discordance complicates pain management and illustrates a need for improved communication.
- OIC symptoms, laxative use and effectiveness, and impact of OIC on pain management and quality of life were not fully appreciated by the patient’s providers.
- These disparate perceptions indicate a need for clinical education and an opportunity for pharmacists to provide education regarding OIC to patients and their providers.


### Impact of OIC

Survey of 513 patients on COT with OIC from United States, Canada, United Kingdom, Germany, Sweden, and Norway.

- Produced 289 text responses on what “straining” meant on quality of life (QOL); 469 text responses on what relief of symptoms of OIC would mean to them.
- OIC secondary to COT for CNCP affects the way patients live their lives in the 3 domains of physical, psychological, and practical implications.


### Prevention of Opioid-Induced Constipation: Emerging and Current Treatments

#### Current Treatments

**Lubiprostone**

- Approved by the FDA in 2013 for the treatment of OIC in adult patients with chronic noncancer pain.
- Selective type 2 chloride channel activator (CIC-2) leading to increases in intestinal fluid secretion, leading to increased gut motility.
- Dosing: 24 mcg twice daily and should be administered with food.
- ADRs: nausea, diarrhea, headache, abdominal pain and distension, and flatulence.


#### Current Treatments

**Oxycodone/Naloxone**

- Naloxone, administered orally, acts locally on mu opioid receptors in the GI tract.
- Oxycodone and naloxone administered in a ratio of 2:1 has been shown to relieve constipation and is associated with few adverse effects. It has also been associated with improvements in quality of life.
- ADRs: nausea, vomiting, headache, constipation, and diarrhea.


#### Current Treatments

**Tapentadol**

- Mu-opioid agonist that also inhibits the reuptake of norepinephrine, contributing to its analgesic effect.
- In a study involving 343 patients with cancer, the incidence of gastrointestinal treatment-associated adverse events was lower in the tapentadol group (55.4% [93/168]) than in the oxycodone group (67.4% [116/172]).
- ADRs: nausea, vomiting, dizziness, drowsiness, fatigue, headache.

Prevention of Opioid-Induced Constipation: Emerging and Current Treatments

Current Treatments
Mu-opioid receptor antagonists
- Designed to inhibit the peripheral effects of opioid medications in the GI tract without reducing analgesia or inducing opiate withdrawal
- Act locally to inhibit opioid binding in the GI tract
- Methylnaltrexone: should be used with caution in patients with gastrointestinal perforation, severe and persistent diarrhea, and disruptions in the blood brain barrier
- ADRs: abdominal pain, flatulence, nausea, vomiting, dizziness, diarrhea, and hyperhidrosis


Naloxegol
- Does not cross blood brain barrier; potential for drug-drug interactions with centrally acting opioids is limited
- Is a CYP3A4 and P-gp substrate; the dose of naloxegol should be reduced by 50% when prescribed with CYP3A4 inhibitors
- Contraindicated in patients at risk or with GI obstruction due to an increased risk for perforation
- ADRs: abdominal pain, diarrhea, nausea, headache, and flatulence


Naldemedine
- Evaluated in the COMPOSE clinical trial program, which examined the effectiveness and safety of naldemedine with placebo in patients with OIC and chronic, noncancer pain
- Naldemedine was associated with a statistically significant improvement in the frequency of BMs per week compared with placebo; after 52 weeks, revealed long-term safety with no statistically significant signs or symptoms of opioid withdrawal
- ADRs: similar to other agents in group


Axelopran: mu receptor antagonist being developed for the treatment of OIC

Quality Indicators in Pain and OIC Management

With the increase in prescribing of opioid medication for COT in CNCP, health plans and accrediting agencies such as JCAH needed an objective method to assess performance of providers and hospitals and the treatment of adverse effects of opioid medication.

Bowel Function Index (BFI): questionnaire that assesses ease of defecation, feeling of incomplete evacuation, and patient's personal judgment of constipation
- BFI score change of at least 12 points is considered a clinically significant change in constipation

Quality Indicators in Pain and OIC Management

Patient-Reported Outcome Assessment Tools
- Bowel Function Index (BFI): questionnaire that assesses ease of defecation, feeling of incomplete evacuation, and patient's personal judgment of constipation
- BFI score change of at least 12 points is considered a clinically significant change in constipation
Quality Indicators in Pain and OIC Management

Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS)

• This rating system measures patients’ perspectives on hospital care in 8 domains such as doctor communication, care transition, discharge information, and pain management
• Health systems should ensure they have processes and resources (eg, staff, equipment, facilities) in place to regularly assess, monitor, and follow up on pain diagnoses according to Joint Commission Standard


Pharmacists’ Role in OIC Prevention and Treatment

• Identify the signs and symptoms of OIC and recognize when uncontrolled pain may be due to medication nonadherence
• Provide clinical recommendations about appropriate treatment when OTC agents are ineffective
• Assist with formulary management decisions
• Assist with improving the rating of the HCAHPS surrounding pain management

Best Practice Guidelines for OIC

• https://www.practicalpainmanagement.com/opioid-induced-constipation-causes-treatments

Pharmacists’ Role in OIC

• Always remember that OIC can occur as long as your patient is taking opioid medication. Therefore, a bowel regimen should always be present for the duration of opioid therapy. This is often forgotten.
• Ask your patients directly if they are having problems with constipation.
• Use any laxative or medication designed to combat constipation carefully in the setting of IBD, or if the patient has an acute change in bowel habits.

Pharmacists’ Role in OIC

• Be familiar with your patient’s health plan criteria for use with these newer OIC agents
• Be aware that mu-opioid antagonists have a small chance of including opioid withdrawal
• Be familiar with the fact that one-third of patients on chronic opioid therapy alter their opioid therapy secondary to OIC, possibly contributing to a perceived lack of efficacy of the opioid therapy at the current dose, possibly leading to an increase in opioid dose, leading to more OIC…and so on…
Opioid prescribing has increased; as such, OIC has increased. Pharmacists are in an ideal position to assess patients for non-adherence, monitor for drug-drug interactions, monitor for appropriate dosing of agents, monitor for ADRs, provide medication recommendations, formulate recommendations, and most cost-effective therapy.

### Conclusion

- Opioid prescribing has increased; as such, OIC has increased.
- OIC is the most common GI opioid ADR, which can lead to non-adherence.
- There are multiple agents available to treat OIC when laxatives do not work.
- Pharmacists are in an ideal position to assess patients for non-adherence, monitor for drug-drug interactions, monitor for appropriate dosing of agents, monitor for ADRs, provide medication recommendations, formulate recommendations, and most cost-effective therapy.

### Additional References

For healthcare professionals:

### Additional Resources

For patients:
1. https://paincommunity.org/resources/managing-opioid-induced-constipation/
5. https://www.theacpa.org/treatment/opioid-induced-constipation

### Additional References