Adverse Effects Associated with Opioid Analgesics

1. Managing Adverse Effects of Opioid Analgesics

1.1 Audio Instructions

The course contains audio.
Turn on your speakers
or plug in your headphones.

1.2 Welcome

Adverse Effects Associated with Opioid Analgesics

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1.3 Introduction

**Introduction**

- Opioids are the mainstay treatment for both malignant and non-malignant pain syndromes
- A variety of adverse effects to opioids exist ranging from mild to severe
- Side effects assessment and management is a key component of pain management
- Patient and family education on potential side effects can provide reassurance and prompt early reporting of symptoms to care providers
- Practitioners at every level must be aware of the most common adverse effects in order to prevent, monitor, and treat symptoms appropriately

1.4 Are Opioids the Culprit?

**Are Opioids the Culprit?**

- Common adverse effects of opioids may also be manifestations of underlying disease or other treatments
- Symptoms may be related to acute medical changes (e.g. infection, obstruction, organ dysfunction)
- Side effects should not be deemed entirely opioid-related
- Differential diagnoses must be considered

[View Reference]
## 1.5 Potential Side Effects of Opioids

### Potential Side Effects of Opioids

- Constipation
- Somnolence
- Delirium
- Respiratory Depression
- Nausea and Vomiting
- Myoclonus

## 1.6 Opioid-Induced Constipation

### Opioid-Induced Constipation

- Among the most common and persistent side effects of opioids
- Tolerance to constipation does not typically develop with repeated opioid use
- Prevalence ranges from 20%-80% depending on diagnosis
- Cause is often multi-factorial and should be investigated
- Opioids impair normal gastrointestinal function by:
  - Decreasing peristalsis
  - Facilitating reabsorption and inhibiting secretion of fluid and electrolytes into the intestinal lumen
  - May also prevent sphincter relaxation required for defecation
1.7 Management of Constipation

Management of Constipation

- Lifestyle modification and prophylaxis are essential when initiating opioids
- Stimulant laxatives (e.g., bisacodyl, senna) are first-line therapy for opioid-induced constipation
- Bulk-forming laxatives not indicated for opioid-induced constipation
- Opioid receptor antagonists - three different agents available
  - Work locally in the gut as peripheral opioid receptor antagonists while sparing actions mediated by centrally-located receptors
  - Cost is a limiting factor in clinical use

1.8 Traditional Agent Selection in Constipation

Traditional Agent Selection in Constipation

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emollients (Softening)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Docusate</td>
<td>1-3 days</td>
<td>50-500 mg 1-4 divided doses</td>
</tr>
<tr>
<td>Osmotic Stimulants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mg Citrate</td>
<td>3-6 h</td>
<td>150-300 mL</td>
</tr>
<tr>
<td>Mg Hydroxide</td>
<td>30 min-6 h</td>
<td>5-15 mL q6h</td>
</tr>
<tr>
<td>Polyethylene glycol</td>
<td>24-96 h</td>
<td>17 g once – three times daily</td>
</tr>
<tr>
<td>Lactulose</td>
<td>24-48 h</td>
<td>30 mL 1-2 times daily</td>
</tr>
<tr>
<td>Sorbitol</td>
<td>30 min -1 h</td>
<td>30 mL</td>
</tr>
<tr>
<td>Contact Stimulants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bisacodyl</td>
<td>6-12 h</td>
<td>5-15 mg single dose</td>
</tr>
<tr>
<td>Senna</td>
<td>6-12 h</td>
<td>2 tablets (Max 12 tabs/day)</td>
</tr>
<tr>
<td>Pro-kinetic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>1 h</td>
<td>10 mg q6h</td>
</tr>
</tbody>
</table>
1.9 Somnolence

Somnolence

- More common with opioid initiation or rapid titration
- Initial sedation should subside within days to weeks
- Patients and families should be made aware of the potential for sedation to prevent abrupt cessation of opioids
- May limit ability to titrate opioids to desirable analgesic effect

1.10 Management of Somnolence

Management of Somnolence

- Medication reconciliation to identify other sedating agents
- Assessment for potential contributing factors (infection, insomnia leading to daytime sleepiness, etc.)
- If analgesia is satisfactory, opioid dose reduction by 25% may alleviate symptoms
- If there is unsatisfactory analgesia preventing dose reduction and significant sedation, consider opioid rotation taking into account incomplete cross-tolerance
- Psychostimulants (e.g., methylphenidate, modafinil) may be considered, however, limited data exists to support use
1.11 Delirium

Delirium

- Disturbance in consciousness: altered awareness, impaired attention, changes in cognition
- Result of accumulation of opioid metabolites
- Typical triad of delirium precipitants include:
  - Opioids, other psychoactive medications
  - Infection
  - Volume depletion, dehydration
- More severe cases associated with myoclonus, hyperalgesia, allodynia

1.12 Treatment of Delirium

Treatment of Delirium

- Consider the various etiologies of cognitive dysfunction in advanced illness
- Prompt evaluation and treatment helps to resolve easily correctable factors
- If opioids are deemed to be the primary culprit, consider dose reduction or rotation to an alternate agent when appropriate
- Pharmacologic management for symptomatic relief includes the use of neuroleptics or other sedating agents (e.g. haloperidol, chlorpromazine, olanzapine)
1.13 Respiratory Depression

Respiratory Depression

- One of the most serious and feared side effects of opioids
- Rare in opioid-tolerant patients and when opioids are used judiciously
- More common during acute initiation of opioids, rapid escalation, and in some cases rotation
- In most cases, increased sedation precedes respiratory depression
- Thorough evaluation is essential to avoid improper use of opioid antagonists

1.14 Management of Respiratory Depression

Management of Respiratory Depression

- Use of naloxone, an opioid antagonist, is indicated when respiratory rate is less than eight breaths/min or hypoxemia (oxygen saturation <90%)
- Slow titration in order to reverse effects of opioids
- Rapid administration can result in abrupt withdrawal and unnecessary patient distress
- Repeated doses may be needed due to the short duration of action of naloxone
- Check individual hospital policies for administration guidelines
1.15 Nausea and Vomiting

Nausea and Vomiting

Common with opioids due to effects on the chemoreceptor trigger zone (CTZ), vestibular sensitivity, and delayed gastric emptying

Observed in up to 30% of patients started on opioids

Habituation usually occurs within several days

Review medication list to rule out other causes

Anti-emetics should be selected based on suspected physiologic mechanism of nausea/vomiting

1.16 Management of Nausea and Vomiting

Management of Nausea and Vomitting

- Opioid dose reduction or rotation if appropriate

- Delayed gastric emptying
  - Prokinetic Agents (e.g., metoclopramide)

- Vestibular sensitivity
  - Antihistamines (e.g., meclizine, hydroxyzine)
  - Anticholinergics (e.g., hyosine, scopolamine)

- Chemoreceptor Trigger Zone (CTZ)
  - Selective 5HT3 receptor antagonists (e.g., ondansetron, granisetron, palonosetron)
  - Phenothiazines (e.g., prochlorperazine, chlorpromazine)
  - Butyrophenones (e.g., Haloperidol, Droperidol)
1.17 Myoclonus

Myoclonus

- Myoclonus is an uncontrollable twitching and jerking of various muscle groups
- Associated with higher doses of opioid therapy
- Evidence suggests association with metabolite accumulation, particularly in organ dysfunction
- Convulsant effects have been associated with preservative in parenteral opioid infusions

1.18 Managing Myoclonus

Managing Myoclonus

- Opioid rotation may be indicated
- Benzodiazepines (e.g., clonazepam, lorazepam, diazepam)
- Prophylactic administration of anticonvulsants generally not warranted
- Preservative-free solutions should be considered when administering high-dose opioid infusions
1.19 Other Potential Side Effects of Opioids

Other Potential Side Effects of Opioids

- Pruritis
- Sweating
- flushing
- Hyperalgesia/allodynia
- Dry mouth
- Urinary retention

1.20 Summary

Summary

Opioid therapy is a mainstay of malignant and non-malignant pain management

Global assessment of pain requires awareness and knowledge of potential side effects of opioids and general management strategies

Patients and families should be educated on symptoms and expected timeline of resolution to ensure compliance and optimal pain management throughout the disease trajectory

Awareness of the side effects profile of opioids can alleviate provider’s fear of opioid prescribing and improve patient outcomes
1.21 Education Partners

Education Partners

ASCO®
AMERICAN SOCIETY OF CLINICAL ONCOLOGY

APAÒ
ASSOCIATION OF PHYSICIAN ASSISTANTS IN ONCOLOGY
partners in cancer care

APSHO
Advanced Practitioner Society for Hematology and Oncology

HOPA
Hematology/Oncology Pharmacy Association

1.22 Thank you!
2. Learning Objectives

2.1 Learning Objectives

- Describe the assessment, prevention, and treatment of the following adverse effects that can be associated with opioid therapy: constipation, somnolence, delirium, respiratory depression, nausea and vomiting, and myoclonus.
- Discuss the process of differential diagnosis as it relates to determining causation of symptoms experienced.