1.12 Opioid Side Effects

Key Points

1. Treatment of pain with opioids includes monitoring for multiple side effects. Opioid side effects include sedation, constipation, nausea/vomiting, delirium, urinary retention, multifocal myoclonus, respiratory depression, withdrawal/physical dependence, acetaminophen or aspirin overdose, cost and diversion of medications. Have medications available to manage side effects.

2. As a general rule, begin with short-acting opioids and switch back to them with the development of dehydration or renal/hepatic failure or during the active dying phase.
   Review other medications when starting opioid. Pay special attention to dosing when oral route no longer possible.

3. The benefit of pain relief may outweigh the burden of side effects that cannot be completely controlled.

4. Constipation, which is not self-limiting, is a side effect of opioids.
   Constipation is easier to prevent than to treat. Counter constipation with a large-bowel stimulant such as Biscodyl or Senna. Goal is a bowel movement at least QOD.

5. Delirium is a side effect of opioids.
   Counter delirium by considering other causes and rotation of opioid to short-acting form. The physician may need to treat through the delirium if the option is poorly controlled pain.

6. Respiratory depression is a rare side effect of opioids, usually occurring only in opioid-naive patients in whom tolerance develops quickly.
   Begin with short-acting opioids and small doses. Sedation usually precedes respiratory depression.

7. Cost/access barriers to procuring opioids can lead to pseudo-addictive behaviors.
   Patients may have difficulty affording opioids; generic drugs are usually less expensive. Patients may have difficulty accessing opioids because of the requirement for a written refill, Medicaid/insurance limits on maximum doses, failure of pharmacies to carry certain medications, and time limits on frequency of refills that may preclude a prescribed dose escalation.

Opioid Side Effects

The Palliative Response

Types of Opioids

- Tylenol/Codeine (Tylenol #3™)
- Tylenol/Hydrocodone (Lortab™)
- Tylenol/Oxycodone (Vicodin™, Percocet™)
- Aspirin/Oxycodone (Percodan™)
- Propoxyphene (Darvon™, Darvocet™)
- Methadone (Dolophine™)
- Morphine (MS Contin™, Oromorp™, Roxicet™, Roxinol™)
- Hydromorphone (Dilaudid™)
- Fentanyl (Duragesic™)

Opioid Routes and Forms

- Oral
- Sublingual
- Subcutaneous
- Rectal
- Topical
- Intramuscular
- Intravenous
- Intraspinal
- Liquid
- Concentrate
- Immediate release
- Sustained release
- Suppository
- Injection
- Infusion
- PCA (patient-controlled)

Factors That May Affect Opioid Dosing

- Renal failure
- Hepatic failure
- Advanced age
- History of substance abuse
- Concomitant medications
- Dehydration
- Route
- Last hours of life

Side Effects to Monitor

- Sedation
- Constipation
- Nausea/vomiting
- Delirium
- Urinary retention
- Myoclonus, multifocal
- Respiratory depression
- Withdrawal/physical dependence
- Tylenol overdose
- Aspirin overdose
- Cost
- Diversion of medications

General Principles of Side-Effect Management

- Anticipate side effects

  Have medications available to manage
- Warn/counsel patients about side effects

  Many side effects are self-limiting

  Call-back may be helpful at 24–48 hours to advise patients about management of opioids

  Counsel against exceeding 4 grams Tylenol/24 hours (Many patients are not aware that they should not use Tylenol and combination opioids together)

General Principles of Opioid Dosing

- Initiating opioids
  Review medications when starting opioid
  As general rule, begin with short-acting opioids and convert to sustained-release after a dose finding
- Switch back to short-acting opioids when:
  Dehydration develops
  Renal or hepatic failure develops
  Patient is in the actively dying phase
- Special attention to dosing when oral route no longer possible

Opioids
Burden versus Benefit

- Some side effects will develop during treatment of pain with opioids
- Patient and healthcare provider should discuss ways to minimize side effects
- However, the benefit of pain relief may outweigh the burden of the side effects if they cannot be completely controlled

Opioid Side Effect: Sedation

- Many patients who have been sleep-deprived by poorly controlled pain, sleep more than usual in the first few days after starting an opioid
- Sedation is usually self-limiting

Countering Sedation

- Discontinue or reduce other sedating medications when feasible
- Consider switching to shorter-acting opioids if pharmacological accumulation is of concern
- Reduce dose
- Consider methylphenidate 2.5–5mg 2 or 3 times during day
- Discuss patient's preference for sedation versus level of pain control

Opioid Side Effect: Constipation

- Not a self-limiting side effect
- Goal: Prevent versus treat
  Start a laxative when start an opioid
  Consider discontinuing or altering other medications that may cause constipation
- Countering constipation
  Use a large-bowel stimulant as a laxative (e.g., biscodyl or senna)
  Goal is a bowel movement at least QOD

Opioid Side Effect: Nausea/Vomiting

- Usually self-limiting
- Action of opioids
  Affect chemoreceptor trigger zone
  Delay gastric emptying

Countering Nausea/ Vomiting

- Consider premedicating
  Use caution about sedating effects of combination treatment
- Consider metochlopromide or haloperidol
- For persistent nausea/vomiting, rotate to alternative route or equivalent dose of another opioid

Persistent Nausea/ Vomiting
Differential Diagnosis

- Other medications
- Constipation
- Obstruction
- Progression of the illness

Opioid Side Effect:
Urinary Retention

- High-risk patients – monitor for retention
  History of retention
  BPH in elderly
  Patients on medications (e.g., anticholinergics) that may contribute to urinary retention
- Countering urinary retention
  Foley catheter
  Consider stopping other medications
  Treat infection
  Treat with Terazosin (Hytrin)

Opioid Side Effect:
Multifocal Myoclonus

- Countering Multifocal Myoclonus
  Opioid rotation
  Reduce dose if pain will allow
  Try to maintain hydration
  Stop long-acting and continuous opioids
  Benzodiazepines
- Differential diagnosis
  Consider that renal or hepatic dysfunction may be developing

Opioid Side Effect:
Delirium

- Consider and treat other causes for delirium
- Treat delirium with haloperidol
- Rotate opioid and switch to short-acting form
- Fentanyl
  Has many advantages but…
  May be problematic because of accumulation in lipid-rich areas like the brain
- May need to treat through the delirium if the option is poorly controlled pain

Opioid Side Effect:
Respiratory Depression

- Presentation
  Usually opioid-naive patients
  Tolerance develops quickly
- Prevention
  Begin with short-acting opioids, small doses
- Forewarning
  Sedation usually precedes respiratory depression

Opioid Side Effect: Respiratory Depression

High-Risk Patients

- Treated for acute pain now resolved
- Debilitation
- Neurological impairment
- Respiratory impairment
- New onset of renal or hepatic insufficiency

Respiratory Depression Treatment

- Prevent by holding doses for sedation if pain control is adequate
- Opioid rotation may be helpful (less helpful than for other side effects)
- Naloxone

  Use with caution—can cause acute withdrawal and pain crisis

  10:1 dilution with careful titration

Respiratory Depression Burden versus Benefit

- Some degree of sedation may be acceptable to patient/family in cases where pain is difficult to control

Opioid Side Effect: Withdrawal/Dependence

- Withdrawal effects in patients treated with opioids for chronic pain
- Withdrawal may precipitate

  Pain crisis

  Physical withdrawal
- Examples of withholding

  Complication of disease that prevents oral dosing

  Hospital admission

Opioid Side Effect: Tylenol/Aspirin Overdose

- Overdose from combination opioids

  Patient may take too much acetaminophen secondary to ineffective pain treatment so that they escalate combination opioid unaware of danger
- Overdose from Tylenol/Aspirin

  Patient may add these drugs to a combination out of ignorance about potential results

Opioid Side Effect: Cost/Access Barrier

- Cost barriers
- Access barriers

  Opioids require written refill

  Medicaid/insurance limits on maximum doses

  Many pharmacies do not carry certain medications

  Time limits on frequency of refills (may affect patient who needed a dose escalation during the previous month)
- Barriers can lead to pseudo-addictive behaviors

Selected Readings

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