Learning Objectives

- Evaluate the use of major tranquilizers, sedative-hypnotics, opioids, and reversal agents in order to control pain and minimize adverse responses associated with painful or frightening medical interventions.
- Compare the strengths of opioid and non-opioid drugs in order to achieve the most effective pain management.
- Describe the benefit of more frequent pain assessment.
- Utilize IV opioids as the preferred method of narcotic analgesia in the emergency room, since they are faster acting and easier to titrate.

Additional Points

- Describe the basic pharmacology of opioids.
- Identify strategies for the management of a pain crisis.
- Recognize opioid conversion factors.
- Identify the levels of sedation.
- Describe at least three methods for conscious sedation.

Physicians Underestimate Symptom Burden

- Therefore we undertreat
- Physicians only overestimated symptom burden in 1% of their patients

Pain and Sedation

General Principles of Pain

- Assessment
  - History
  - Physical
- Management
  - Rx underlying cause
  - Pharmacologic
  - Non-pharmacologic
- Education
  - Patient
  - Family
  - All caregivers
- Regular review
  - Assess outcomes
  - Plan of care
- Transdisciplinary care
- Consultative expertise

Defining Pain

- An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage

Audience Response System

What are the two types of pain?

- Direct and indirect
- Physiologic and supratentorial
- Acute, subacute and chronic
- Nociceptive and neuropathic

Types of Pain

- Nociceptive
- Neuropathic

Nociceptive Pain

- Transduction – direct stimulation of intact nociceptors
  - Mechanical – pressure, stretch
  - Temperature
  - Chemical
- Transmission along normal nerves

Neuropathic Pain

- Disordered peripheral or central nerves
- Compression, transection, infiltration, ischemia, metabolic injury
- Varied types
  - Peripheral, central, deafferentation, complex regional syndromes
Pain and Sedation

Pain Assessment
- Location
- Quality (type)
  - Nociceptive
  - Neuropathic
  - Mixed
- Temporal profile
- Severity
- Effect of medications / therapies
  - Benefit
  - Adverse

Temporal Profile
- Constant
- Breakthrough
- Intermittent

Pain Scales
- Numeric
- Faces
- PAINAD scale

PAINAD Scale
- PAINAD scale...
  - Breathing independent of vocalization
  - Negative vocalization
  - Facial expression
  - Body language
  - Consolability

WHO Stepladder
1 mild (1-3)
  - Acetaminophen
  - ASA / NSAIDs
  ± Adjuncts

2 moderate (4-6)
  - A / Codeine
  - A / Hydrocodone
  - A / Oxycodone
  - Tramadol
  ± Adjuncts

3 severe (7-10)
  - Morphine
  - Fentanyl
  - Hydromorphone
  - Methadone
  - Oxycodone
  ± Adjuncts

Perspectives on Dosing
- 1 A/Hydrocodone = 5 mg immediate-release oral morphine
- 1 A/Oxycodone = 8 mg immediate-release oral morphine
- Fentanyl patch 25 mcg/hr = 50 mg oral morphine
Pain and Sedation

**Opioid Conversion**
- Oral to IV morphine 3:1
- Oral morphine to IV hydromorphone (Dilaudid) 15:1
- Oral to IV hydromorphone 3:1
- Oral to IV methadone 3:1
- Fentanyl 25 mcg patch = Oral morphine 50 mg per day

**Case Example**
- 72 yo male presents to the ED c/o lumbar spine pain. Patient has metastatic prostate cancer. His home pain regimen includes 120 mg extended-release morphine q 12 hours and 20 mg immediate-release morphine q 1h PRN breakthrough pain. He has had 11 breakthrough doses in the past 24 hours.

**Audience Response System**
What would be the initial bolus dose of IV morphine in the ED?
- a. 4 mg
- b. 10 mg
- c. 15 mg
- d. 20 mg

**Case Example Continued**
- First calculate the patient’s total daily morphine dose
  - 120 mg x 2 = 240
  - 20 mg x 11 = 220
  - Total daily dose = 460 mg oral morphine
- Next convert to IV morphine
  - 460/3 = 153 mg IV morphine
  - 10% for bolus would be 15 mg IV morphine

**Audience Response System**
How many minutes does it take for A/Oxycodone or A/Hydrocodone to reach maximum concentration in your bloodstream?
- a. 30 minutes
- b. 60 minutes
- c. 90 minutes
- d. 240 minutes

**Pharmacology**
- For codeine, morphine, hydromorphone, oxycodone and hydrocodone
  - Cmax PO=1 hour
  - Cmax PR=1 hour
  - Cmax IM=30 minutes
  - Cmax SQ=30 minutes
  - Cmax IV=10 minutes
  - Half life=4 hours
Pain and Sedation

Morphine Metabolism

MORPHINE → liver
- M3G
- M6G

MORPHINE → kidney
- M6G
- M3G

URINE

Analgesia
- CNS
- +++
- M6G
- +++
- M3G

Urine output
- < 500 mL / 24 hr
  - routine dose by 50%
- < 250 mL / 24 hr
  - stop routine dose.
  - continue PRN dosing

Audience Response System

What is the most common side effect of opioids from the following list?

a. Hallucinations
b. Respiratory depression
c. Pruritus
d. Constipation

Opioid Side Effects

- Common
  - Constipation
  - Dry mouth
  - Nausea / Vomiting
  - Sedation
  - Sweats
- Uncommon
  - Bad dreams / Hallucinations
  - Dysphoria / Delirium
  - Myoclonus / Seizures
  - Pruritus / Urticaria
  - Respiratory depression
  - Urinary retention

Treatment of Constant Pain

- Dose once every half life
  - Steady State of the drug is reached in 5 half lives
- Give breakthrough dosing for excess pain
  - Breakthrough gets dosed on the Cmax
  - Give 10% of 24-hour total for breakthrough dose

Pain Crisis Management

- Use IV medications
- Use a logical starting dose, either calculate or give a weight-based dose of morphine = 0.1mg/kg
- Reassess the patient every 10 minutes (Cmax for IV meds)
- If patient still in severe pain, double the dose every 10 minutes

Case Example

- A 34 yo male presents to the ED with hx of malignant melanoma. Is complaining of 10/10 pain. His current pain regimen includes hydromorphone 12 mg PO q 4 hours atc and hydromorphone 8 mg PO q 1 hour PRN. He has had 15 PRN doses in the past 24 hours.
Pain and Sedation

Audience Response System
What is the initial IV bolus of hydromorphone?
- a. 2 mg
- b. 4 mg
- c. 6 mg
- d. 8 mg

Audience Response System
When you re-evaluate this patient in 15 minutes, his pain is still 10/10. What is the most appropriate dose of IV hydromorphone?
- a. 12 mg
- b. 10 mg
- c. 6 mg
- d. 20 mg

Four Levels of Sedation
- Minimal Sedation (anxiolysis)
  - Normal response to verbal stimulation
  - Airway is unaffected
  - Spontaneous respiration
  - Unaffected cardiovascular function

Four Levels of Sedation
- Moderate Sedation (conscious sedation)
  - Purposeful response to verbal or tactile stimulation
  - No airway intervention is required
  - Spontaneous ventilation is adequate
  - Cardiovascular function is usually maintained

Four Levels of Sedation
- Deep Sedation
  - Purposeful response after repeated painful stimuli
  - Airway intervention may be required
  - Spontaneous ventilation may be inadequate
  - Cardiovascular function is usually maintained
## Pain and Sedation

### Four Levels of Sedation

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
</table>
| General Anesthesia | - Unarousable even with painful stimulus  
- Airway intervention is required  
- Spontaneous ventilation is inadequate  
- Cardiovascular function may be impaired |

### ASA Classification of Patients

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>The patient is normal and healthy</td>
</tr>
<tr>
<td>II</td>
<td>The patient has mild systemic disease that does not limit activities</td>
</tr>
<tr>
<td>III</td>
<td>The patient has moderate or severe systemic disease that does not limit activities</td>
</tr>
<tr>
<td>IV</td>
<td>The patient has severe systemic disease that is a constant threat to life</td>
</tr>
</tbody>
</table>

### Is Conscious Sedation Necessary?

- **Anterior Shoulder Dislocations**
  - Compared 20 mL of 1% intraarticular lidocaine to opioid and benzodiazepine combination
  - No statistical significance in success rate of reduction
  - No statistical significance in patient’s pain
  - Lidocaine group had shorter length of stay
  

### Is Pre-Oxygenation Necessary?

- **A randomized controlled trial**
  - Patients received oxygen 2L/min via NC versus compressed air
  - No difference for respiratory depression
  - No difference for hypoxia
  

- **A randomized controlled trial**
  - All patients received propofol at 1 mg/kg followed by 0.5 mg/kg until adequate sedation achieved
  - One group received oxygen 15L via NRB
  - One group received compressed air
  - Hypoxia in 19% of patients with oxygen versus 41% in compressed air
  

- **A randomized controlled trial**
  - All patients received propofol for sedation
  - One group received oxygen 3L/min via NC
  - One group received compressed air
  - Oxygen group had hypoxia 18%
  - Compressed air had hypoxia 28%
  
Propofol

- Intravenous nonbarbiturrate anesthetic
- Induction is as quick as thiopental, but emergence is 10 times more rapid
- Dose is 1-2 mg/kg IV
- Inhibits NMDA subtype of glutamate receptors and agonizes GABA-A receptor
- Undergoes rapid metabolism in the liver and is excreted by the kidneys

The Safety of Propofol

- Prospective, observational, multicenter study
- 82 procedural sedations using propofol
- 11% had brief hypoxemia with average time of hypoxemia lasting 1.2 minutes
- No advanced airway maneuvers performed

Ketamine

- A sedative hypnotic
- Produces both sedation and analgesia
- Non-competitively blocks NMDA receptors
- Acts on receptors in the cortex and limbic systems
- Has sympathomimetic activity
- Metabolized in the liver
- Excreted by kidneys

Ketamine Dosing

- 1 mg/kg intravenous
- 2 mg/kg intramuscular

Can Patients Control the Amount of Propofol They Receive?

- Randomized controlled trial of patients who received propofol dosing at the EP discretion versus one loading dose and then patient controlled sedation
- Trend toward lower dosing with patient controlled sedation
- No difference in adverse events, success rate, ease of procedure

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Ketamine Emergence Reaction

- The No. 1 side effect of ketamine
- Randomized controlled trial to see if adding midazolam reduces the incidence
- Subjects received 1.5 mg/kg IV ketamine alone versus ketamine and 0.03 mg/kg midazolam IV
- Those who received midazolam experienced emergence 8% versus 25%


Ketamine-Propofol (Ketofol)

- Randomized, double-blind, placebo controlled trial
- All patients received IV fentanyl and then either ketamine 0.5 mg/kg IV or placebo followed by propofol 1 mg/kg IV
- There was no difference in respiratory depression
- With ketamine-propofol, physicians and nurses were more satisfied and used less propofol


Etomidate

- Short-acting, intravenous, sedative hypnotic without analgesic properties
- Facilitates GABAergic neurotransmission by increasing the number of available GABA receptors
- Metabolized by the liver
- Excreted by the kidneys


Etomidate Versus Midazolam

- Prospective, randomized, double-blind trial
- Patients received either etomidate 0.1 mg/kg IV or midazolam 0.03 mg/kg IV alone
- Total sedation time was less for etomidate, 15 minutes, versus 32 minutes for midazolam
- No difference in total length of stay
- Equal in sedation effect


Etomidate Versus Propofol

- Randomized controlled trial
- Patients received either etomidate or propofol alone
- Respiratory depression in 34% of etomidate patients versus 42% of propofol patients
- Myoclonus occurred in 20% of etomidate patients

Thank You for Your Time and Attention

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