Lesson 6.1
Opioid (Narcotic) Analgesics and Antagonists

1. Explain the classification, mechanism of action, and pharmacokinetics of opioids.
2. List and describe the pharmacologic effects and potential adverse reactions of opioids.
3. Discuss the addiction potential of opioids, including treatment.
4. Name and explain the analgesic actions of the most common opioid agonists.
5. Discuss the actions of and provide examples of the mixed opioids.
6. Summarize the mechanism of action and adverse reactions of tramadol.
7. Apply the use of opioids to dentistry.
Introduction

- Opium – dried juice from the unripe seed capsules of the opium poppy
- 1800s – morphine and codeine were isolated from opium
- Until 1920 – medications containing opium were promoted
- Oral opioids became unlawful – injection abuse began and continues today

Classification of Opioid Analgesics & Antagonists

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<tr>
<th>Group</th>
<th>Subgroup</th>
<th>Example</th>
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<tr>
<td>Agonists</td>
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<td>Mu-agonists</td>
<td>Partial agonists</td>
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Mechanism of Action

- Enkephalins
- Endorphins
- Dynorphins
- Important receptors include:
  > Mu (μ)
  > Kappa (κ)
  > Delta (δ)
Pharmacokinetics

- ADME
  - Absorption
  - Distribution
  - Metabolism
  - Excretion

Pharmacologic Effects

- Analgesia
- Sedation and euphoria
- Cough suppression
- Gastrointestinal (GI) effects
- Adverse reactions

Pharmacologic Effects (Cont.)

- Morphine
- Oxycodone
- Hydrocodone
- Codeine
Pharmacologic Effects (Cont.)

- Sedation and euphoria
  - *κ* receptor stimulation
  - Potentiate analgesic effect; relieve anxiety
  - Additive with other CNS depressants
  - Remove pain; euphoria results

Pharmacologic Effects (Cont.)

- Cough suppression
  - Depresses cough center in medulla
  - Antitussive effect requires lower dose
- Gastrointestinal effects
  - Increases the smooth muscle tone
  - Decreases GI’s propulsive contractions and motility

Adverse Effects:

- Respiratory Depression
  - Cause of death with overdose
  - Elderly – decrease in pulmonary ventilation
  - Reduced ventilation produces vasodilation
  - Vasodilation results in intracranial pressure
  - Mask CNS diagnostic symptoms
  - Hyperthyroidism
  - Hypothyroidism
Adverse Reactions: Nausea and Emesis
- Constipation
- Miosis
- Urinary retention & antidiuretic effect
- CNS effects
  - Anxiety
  - Restlessness
  - Nervousness
  - Dysphoria

Adverse Reactions: Cardiovascular Effects
- Biliary tract constriction
- Histamine release
- Pregnancy and nursing considerations
  - FDA pregnancy category C – morphine, codeine
  - Infant born to addict
  - Depressed respiration
  - Withdrawal symptoms

Allergic Reactions
- Dermatologic
  - Skin rashes
  - Urticaria
  - Contact dermatitis
- Some brands of opioid analgesic combinations are formulated with sodium bisulfate – be aware of sulfite hypersensitivity
Drug Interactions

- Sedation
- Respiratory depression
- Interact with monoamine oxidase (MAO) inhibitors
- Interact with antipsychotic agents such as chlorpromazine

Adverse Reactions: Addiction and Chronic Administration

- Two signs of addiction
  - Cravings
  - Loss of ability to stop using & loss of ability to control amount
- Chronic administration
  - Tolerance occurs except to miosis and constipation
  - Habituation
  - Dependence

Adverse Reactions: Addiction

- Degree of addiction potential is proportional to analgesic strength
- Dependent on the drug’s ability to produce euphoria and reduce anxiety
- Length of administration
- Development of tolerance – related to drug strength and frequency of use
Slide 19

Treatment
- Substituting oral opioid for injectable form
- Cold turkey – abrupt withdrawal
- Methadone maintenance
- Administering naltrexone (Trexan)

Slide 20

Specific Opioid Analgesics & Antagonists
- Opioid agonists
  - Morphine
  - Oxycodone
  - Oxymorphone
  - Hydrocodone, Hydrocodone ER
  - Codeine
  - Meperidine
  - Hydromorphone
  - Methadone
  - Fentanyl family
- Mixed opioids
  - Agonist-antagonist
  - Partial agonists
  - Antagonists
  - Pentazocine
  - Full agonist/reuptake inhibitors
  - Tapentadol
  - Tramadol

Slide 21

Specific Opioids: Morphine
- Prototype
- Parenterally – postoperative pain in hospitalized patients
- Orally – treatment of terminal illnesses
- Sustained-release tablets – outpatient use in terminally ill
Specific Opioids: Oxycodone, Oxymorphone
- Oxycodone + aspirin = Percodan
- Oxycodone + acetaminophen = Percocet, Tylox
- Oxymorphone

Specific Opioids: Hydrocodone
- Hydrocodone > hydromorphone
- Hydrocodone + ibuprofen
- Hydrocodone + acetaminophen
- Hydrocodone ER

Specific Opioids: Codeine
- Meperidine (Demerol)
- Hydromorphone (Dilaudid)
- Methadone (Dolophine)
- Fentanyl family
  - Fentanyl (Duragesic, Sublimaze)
    - Fentanyl (Duragesic) transdermal system
    - Sufentanil (Sufenta)
    - Alfentanil (Alfenta)
Mixed Opioids: Agonist-Antagonist Opioids
- Pentazocine (Talwin) – oral
- Butorphanol (Stadol) – nasal spray
- Butorphanol (Butrans) – transdermal patch
- 50 mg pentazocine + 0.5 mg naloxone = choice street drug

Mixed Opioids: Partial Agonists
- Buprenorphine (Buprenex, Subutex)
  - Schedule III
  - Oral and parenteral use

Mixed Opioids: Opioid Antagonists
- Naloxone (Narcan)
  - Treating agonist or mixed opioid overdoses
- Nalmefene (Revex)
  - Reverse opioid overdose
- Naltrexone (ReVia, Vivitrol)
  - Maintenance of the opioid-free state in detoxified, formerly opioid-dependent patients
  - Used in management of alcohol abstinence
Full Agonist/Reuptake Inhibitors: Tramadol (Ultram)

- μ-Opioid agonist action
- Inhibition of reuptake of norepinephrine and serotonin
- No federal scheduling yet; Schedule IV controlled substance in many states

Considerations for Dental Rx of Opioids

- Analgesics account for 40.2% of Rx for patients aged 18-30 years
- Be aware of prescription abuse
- Be aware of illegal selling of Rx drugs
- NSAIDs manage dental pain
- Dispensing excess amount of opioids per Rx
- Codeine or hydrocodone combinations > oxycodone combinations
- Misconception that limited opioid analgesic use does not lead to addiction

Considerations for Dental Rx of Opioids (Cont.)

- Treatment of chronic orofacial pain
- Refer patient, if necessary
- Assess for current signs of drug abuse
- Monitor for potential signs of drug abuse
- Monitor for pain relief
- See patient in office for treatment
- Limit quantity; no refills
- Be aware of demanding patients
Dental Hygiene Considerations

- Conduct thorough medication/health history
- Determine contraindications or possible drug interaction
- Be aware of nonopioid/opioid combinations
- Remind patients to not supplement with OTC agents
- Avoid use with other sedating drugs
- Patients should avoid making life-changing decisions
- Be aware of patient positioning
- Be aware of signs of addiction or abuse

Patient Instructions for Use of Opioid Analgesics

- Take with a full glass of water
- Take with food to minimize GI irritation
- Use caution with driving because of likelihood of dizziness and drowsiness
- Avoid any situations that require thought or concentration because of the likelihood of sedation
- These drugs can cause xerostomia. Drink plenty of water and avoid caffeinated beverages, juices, and sodas

Questions?