1. GI Pharmacology: Drugs for Constipation & Diarrhea

GI Pharmacology: Drugs for Constipation & Diarrhea

Paul Abourjaily, PharmD
Tufts-New England Medical Center  
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2. Objectives

Objectives

• Illustrate drug mechanisms of action
• Identify most common drug side effects
• Provide examples of each drug type

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3. Drugs for Constipation

Drugs for Constipation

- Bulk forming agents
  - Psyllium, Methylcellulose, Polycarbophil
- Softeners/surfactants
  - Docusate, Mineral oil
- Osmotic agents
  - Saline-based
  - Sugar/alcohol-based
  - Other (PEG solutions)
- Stimulants
  - Bisacodyl, Senna, Cascara
- Miscellaneous
  - Lubiprostone, Tegaserod

4. Bulk-forming Agents

Bulk-forming Agents

- Mechanisms:
  - Source of fiber
    - Enhances stool mass
- Main concerns/toxicities:
  - Bloating & abdominal pain
    - Avoid if suspect obstruction
  - Drug interactions of absorption
5. Bulk-forming Agents

Bulk-forming Agents

• Examples:
  – Natural
    • Psyllium
  – Semi-synthetic
    • Methylcellulose
    • Polycarbophil

6. Softeners/Surfactants

Softeners/Surfactants

• Mechanisms:
  • Lowers surface tension of stool

• Main concerns/toxicities:
  • Specific to mineral oil

• Examples:
  • Docusate
  • Mineral oil
7. Osmotic Agents

Osmotic Agents

- Mechanisms:
  - Osmotically-mediated water retention stimulates peristalsis

- Main concerns/toxicities:
  - Abdominal distension, flatulence
  - For saline-based caution if:
    - Renal or cardiovascular disease
    - Underlying electrolyte disorders or on diuretics
    - Monitor Mg, Phos, K, Na, Ca

8. Osmotic Agents

Osmotic Agents

- Examples:
  - Saline-based:
    - Magnesium citrate
    - Phosphate salts
  - Sugar/alcohol-based:
    - Lactulose, Sorbitol, Mannitol
    - Glycerin (suppositories/enemas)
  - Other:
    - Polyethylene glycol (PEG) solutions

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9. Stimulant Laxatives

Stimulant Laxatives

• Mechanisms:
  – Produce migrating colonic contractions

• Concerns/toxicities:
  • Avoid overuse

  • Phenolphthalein and Danthon-containing products banned by FDA in 1999

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10. Stimulant Laxatives

Stimulant Laxatives

• Examples:
  • Diphenylmethanes
    • Bisacodyl
      • Onset of action oral vs rectal

  • Anthraquinones
    • Aloe
    • Cascara
    • Senna

  • Castor oil

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11. Miscellaneous Agents

**Miscellaneous Agents**

- **Lubiprostone**
  - **Mechanism:**
    - Activates chloride channels within GI tract
      - Increasing intestinal fluid secretion
  - **Concerns/toxicities:**
    - Nausea
    - Abdominal distension & pain
    - Diarrhea & flatulence
    - Headache
    - Avoid in pregnancy

12. Drugs for Constipation

**Drugs for Constipation**

- **Bulk forming agents**
  - Psyllium, Methylcellulose, Polycarbophil
- **Softeners/surfactants**
  - Docusate, Mineral oil
- **Osmotic agents**
  - Saline-based
  - Sugar/alcohol-based
  - Other (PEG solutions)
- **Stimulants**
  - Bisacodyl, Senna, Cascara
- **Miscellaneous**
  - Lubiprostone; Tegaserod
13. Anti-diarrheals

**Anti-diarrheals**

- Bulk forming & binding agents
  - Psyllium, Methylcellulose, Polycarbophil
  - Cholestyramine
  - Bismuth
- Antimotility agents
  - Opioids & derivatives
- Antisecretory agents
  - Octreotide
- Miscellaneous
  - Clonidine; Alosetron

14. Bulk-forming & binding agents

**Bulk-forming & binding agents**

- **Mechanisms:**
  - Source of fiber
    - Enhances stool mass
- **Main concerns/toxicities:**
  - Bloating & abdominal pain
  - Drug interactions of absorption
15. Bulk-forming & binding agents

### Bulk-forming & binding agents

- **Examples:**
  - **Natural**
    - Psyllium
  - **Semi-synthetic**
    - Methylcellulose
    - Polycarbophil
  - **Other agents:**
    - Cholestyramine
    - Bismuth subsalicylate

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16. Enterohepatic Recirculation of Bile Acids

### Enterohepatic Recirculation of Bile Acids

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17. Bile Acid Sequestrants

**Bile Acid Sequestrants**

- **Adverse effects:**
  - Few systemic
  - Primarily GI-related
    - Abdominal pain, bloating, constipation
  - Tooth discoloration
    - Liquids
  - Reduced absorption of fat soluble vitamins

18. Antimotility Agents

**Antimotility Agents**

- **Opioid derivatives:**
  - Diphenoxylate + Atropine
    - High doses (40-60 mg) required to produce analgesia
  - Loperamide
    - Little/no penetration into CNS
19. Other Opioid Derivatives

Other Opioid Derivatives

- Camphorated tincture of opium
  Morphine 0.4 mg/mL
- Deodorized tincture of opium
  Morphine 10 mg/mL

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20. Miscellaneous Agents

Miscellaneous Agents

- Clonidine
  - Centrally acting alpha-2 receptor agonist
- Alosetron
  - 5HT₃ receptor antagonist
    - For women
    - When primary symptom is diarrhea
    - Use restricted due to side effect concerns (ischemic colitis)

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Anti-diarrheals

- Bulk forming & binding agents
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  - Bismuth
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- Miscellaneous
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