Disclosure

- I have nothing to disclose concerning possible financial or personal relationship with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.

Learning Objectives

- List 4 medications for which therapeutic levels are affected by tube feeding.
- Discuss options for managing administration of a specific medication with tube feeding to minimize effects on the medication’s efficacy and safety.
- Identify potential drug-tube feeding interactions and treatment options in a given patient scenario.
“Can I give this drug through the feeding tube?”

Medication-Tube Feeding Interactions

- Physical and chemical effects of tube feeding on a drug that result in altered drug concentrations and response to the therapy
- May lead to treatment failure and adverse reactions

Adapt from: Boullata JI. Handbook of drug-nutrient interactions. 2010
Chan LK. J Parenter Enteral Nutr. 2013

Type and Location of the Feeding Tube

Williams NT. Am J Health-Syst Pharm. 2008
Site of Feeding

<table>
<thead>
<tr>
<th>Gastric</th>
<th>Post-pyloric</th>
</tr>
</thead>
<tbody>
<tr>
<td>■ Easier placement</td>
<td>■ Better for patients with gastric dysfunction, pancreatic, and post-operative feeding</td>
</tr>
<tr>
<td>■ More physiologic feeding</td>
<td>■ May reduce the risk of aspiration</td>
</tr>
<tr>
<td>■ Potential for drug-tube feeding interactions</td>
<td>■ Potential for drug-tube feeding interactions</td>
</tr>
</tbody>
</table>

Category of Interactions

■ Physical - precipitation
■ Pharmaceutical – extended release
■ Pharmacologic – vitamin K and warfarin
■ Physiologic – drugs cause feeding intolerance
■ Pharmacokinetic – absorptive environment
■ Pathophysiologic - unintended responses and disease state

Factors Contributing to Medication - Tube Feeding Interactions

■ Administration-related factors
■ Drug-related factors
■ Formula-related factors
Administration-Related Factors

- **Feeding tube size**
  - Long and smaller-bore tubes have a greater risk of occlusion

1. Williams NT. Am J Health-Syst Pharm. 2008  
2. Boullata JI. Handbook of Drug-Nutrient Interactions. 2010  

---

Patient Case

- A 54 years-old male who admitted to the ICU with cirrhosis. There is a concern of GI bleeding and a physician orders sucralfate via the enteral route in addition to pantoprazole.
- Patient is intubated and receives continuous enteral nutrition via Dobhoff tube (DHT).
- Chest X-ray shows DHT with the tip in the third portion of the duodenum.
- What is a major medication-tube feeding interaction in this case?

---

Administration-Related Factors

- **Site of feeding**: Gastric vs. Post-pyloric
  - Drugs intended for a local effect
    - Antacids, sucralfate, bismuth
  - Absorptive environment
    - Ketoconazole, itraconazole and tetracycline require acidic environment (gastric PH) for absorption
    - Digoxin is acid labile and hydrolyzed in acidic environment

1. Williams NT. Am J Health-Syst Pharm. 2008  
2. Boullata JI. Handbook of Drug-Nutrient Interactions. 2010  
Patient Case (continued)

■ What is a major medication-tube feeding interaction in this case?
  – DHT tip is post-pyloric
  – Sucralfate will not present pharmacological effects
  – Sucralfate interacts with pantoprazole
  – Management:
    ■ Reposition DHT to the gastric if sucralfate will be continued
    ■ Discontinue sucralfate

Drug-Related Factors

Dosage forms: liquid vs. solid dosage forms

■ Liquid preparations
  – Generally preferred
  – Factors need to be considered
    o Volume
    o Sorbitol content - causes GI intolerance
    o Hypertonic medication - causes osmotic diarrhea
    o Viscosity – cause tube occlusion
    o Formulations – microgranular, modified-release

1. Williams NT. Am J Health-Syst Pharm. 2008
2. Boullata JI. Handbook of Drug-Nutrient Interactions. 2010

Drug-Related Factors

■ Solid dosage forms
  – Compressed, immediate-release tablets can be crushed
  – Capsules that contain powder, or beads or pellets that are an immediate release form
  – Liquid-filled soft gelatin capsule

Williams MF. Am J Health-Syst Pharm. 2008
Boullata JI. Handbook of Drug-Nutrient Interactions. 2010
Formula-Related Factors

- High-protein content
  - Case reports of interaction between levodopa and protein in enteral feeding
    - Caused levodopa withdrawal and neuroleptic-like syndrome
    - Amino acid from enteral feeding may compete with levodopa for absorption
  - Suggested management:
    - Separate feeding time and drug administration: bolus or cyclic feeding
    - Limit total daily protein intake – may cause malnutrition
    - Increase dose of levodopa

Specific Drug-Tube Feeding Interactions

- Carbamazepine
- Fluoroquinolones
- Phenytoin
- Warfarin
Carbamazepine

- Limited data
- Enteral feeding may decrease carbamazepine absorption
- Carbamazepine may bind to the feeding tube
- Post-pyloric feeding may cause clinically significant effects

References:
- Williams NT. Am J Health-Syst Pharm. 2008
- Boullata JI. Handbook of Drug-Nutrient Interactions. 2010

Oral vs. NG feeding administration
- No significant differences in pharmacokinetic parameters
- Cmax was lower with NG feeding (p = 0.052)
- Strong correlation between CBZ dose and Cmax after oral administration, but not NG feeding

*NG=nasogastric; CBZ = Carbamazepine

Loss of Carbamazepine Suspension through Nasogastric Feeding Tube

- Compared 12 methods of administrating CBZ suspension via NG tube
  - NG tube size, with/without diluent, type of diluent, and type of flush solution
- For methods with diluent, diluted CBZ 10 mL (200 mg) with 10 mL of diluent
- Significant loss of CBZ in undiluted suspension methods
- Significant losses were associated with diluents and flush solution

References:
Carbamazepine

- Management:
  - Dilute CBZ suspension with an equal volume of sterile water
  - Consider holding the feeding for 2 hours before and after drug administration
  - Monitor drug level
  - Consider alternative therapy

Fluoroquinolones

- Drug dependent
- Available studies are small and have limitations
- Possible mechanisms
  - Bind to cations in enteral feeding
  - Bind to the feeding tube
  - Differences in hydrophilicity
Fluoroquinolones

- Management
  - Consider holding enteral formula for 1 hour or more and 2 hours after the dose, especially with ciprofloxacin
  - Switch to IV formula if possible
  - Consider alternative antibiotics

Management

- Consider holding enteral formula for 1 hour or more and 2 hours after the dose, especially with ciprofloxacin
- Switch to IV formula if possible
- Consider alternative antibiotics
Phenytoin

- A systemic review found that decreased serum phenytoin concentrations associated with enteral feeding
- The exact mechanism is unknown
  - Phenytoin binds to feeding tube
  - Phenytoin binds to enteral formula


Management

- Dilute phenytoin suspension with an equal volume of sterile water
- Switch to IV route if possible
- May consider holding formula for 1-2 hours before and after drug administration
- Monitor phenytoin level
- Consider alternative therapy


Phenytoin Recovery From Percutaneous Endoscopic Gastrostomy Pezzer Catheters After Long-Term In Vivo Administration

Boullata JI. Handbook of Drug-Nutrient Interactions. 2010
Warfarin

- Warfarin interacts with vitamin K content in enteral formulas
  - Most of enteral formulas were reformulated to reduce the vitamin K content
- Feeding tube may compromise the amount of warfarin reaching the patient

Warfarin Management

- Adjust warfarin dose
- Consider holding formula for 1 hour before and after drug administration
- Monitor INR closely
- Consider alternative anticoagulants

Original Communication

Warfarin Bioavailability With Feeding Tubes and Enteral Formula

Mark Kleng, MS, RPh, BCNSP, PhD
Denise Graham, RN, NP, DNS, and Veronica McLernon, MS, RD, CDN

Figure 1. Artificial mouth.

Figure 2. Note how warfarin level of dissolution is not substantially altered by addition of formula, but drops significantly after passed through feeding tube. This occurs with both the injectable and oral liquid formulations.
Patient Case

- A 74 years old female with atrial fibrillation who has been on warfarin 5 mg daily at home.
- Patient is admitted in the ICU due to acute kidney injury.
- DHT is placed and enteral feeding is initiated.
- A physician would like to re-start home dose of warfarin.
- What is the appropriate approach that you would like to do in this patient?

General Recommendations

- Administer drugs by the oral route when possible
- Consider alternative routes if drugs are available (e.g. rectal, transdermal, IV, sublingual)
- Liquid dosage forms are preferred
  - Check sorbitol content and osmolality (if possible)
  - Dilute hypertonic products with 10-30 mL of water
  - Dilute viscous products with 30-50 mL water (1:3 volume/volume)

General Recommendations

- If a solid dosage form is used, select appropriate dosage forms
- Do not mix drugs directly to the enteral feeding formula
- Avoid mixing drugs together
- Administer each drug separately

References:
1. Williams NT. Am J Health-Syst Pharm. 2008
2. Boullata JI. Handbook of Drug-Nutrient Interactions. 2010
General Recommendations

■ Flush the tube with at least 15 mL water before and after administering drugs
  ○ Flush the tube with at least 5-10 mL water between drugs
■ Restart the feeding in a timely manner
■ Consider holding feedings before and after administering specific drugs

Acknowledgment

■ Carol J Rollins, MS, RD, CNSD, Pharm.D., BCNSP

References

References


QUESTIONS?
dongtai@pharmacy.arizona.edu