Drug Nutrient Interactions in Enteral Feeding

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Objectives

At the end of the session the participant shall be able to understand the:

- Different oral drug dosage forms;
- Different types of drug nutrient interactions;
- Complexity for drug administration through a feeding tube; and,
- Importance of applying appropriate techniques to avoid tube obstruction, reduced drug efficacy/increased drug toxicity or occupational health risk.
Outline

- Oral Drug Dosage Forms
- Complications of Administering Medication via Enteral Tube Feeding
- Drug–Nutrient Interactions
- ASPEN Practice Recommendations
Oral Drug Dosage Forms
**Oral Drug Dosage Forms**

- **Solids** – mostly immediate-release products which contain the active drug molecule mixed with excipients but there are new drugs introduced as *modified-release products or as complex formulations*
  - Capsules
    - Soft-gel
    - Hard-gel
  - Tablets
    - Plain
    - Film-coated
    - Enteric-coated
Liquids

- Elixirs
  - clear, sweetened hydroalcoholic solutions intended for oral use and are usually flavored to enhance their palatability
  - Disadvantage: Alcohol is not good for children; contains volatile materials

- Solutions
  - homogenous liquid mixtures where active medication is totally and uniformly dissolved in diluent
  - Disadvantage: Increased potential for drug instability due to hydrolysis or oxidation

- Suspensions
  - Heterogeneous liquids containing poorly soluble active medication floating in a liquid medium that contains suspending or thickening agents
  - Disadvantage: Viscosity and potential for settling out of dispersed particles

- Syrups
  - Disadvantage:
Complications of Administering Medication via Enteral Feeding Tube

- Blockage of enteral tube
  - Precipitation
  - Inappropriate selection of drug dosage form
- Reduced drug effect or increased drug toxicity
  - Drug–drug interaction
  - Drug–food interaction
  - Inappropriate handling or preparation of drug
- Occupational health risk
  - Exposure to drug powders such as cytotoxic drugs
# Types of Drug–Nutrient Interactions

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<thead>
<tr>
<th>Type of Interaction</th>
<th>Effect of Interaction</th>
<th>Associated Factors</th>
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| **Physical**        | Precipitation         | Drug formulation and pH  
Curdling                             Reactive chemical moieties  
Clumping                              Protein complexity  
Clumping                              Time  
Change in consistency                     Temperature  
Duration of exposure                    |
| **Pharmaceutical**  | Loss of drug activity | Alteration of modified dosage form  
Toxicity                                  Administration by a different route than that for which it was designed |
| **Pharmacokinetic** | Loss of drug activity | Happens before the drug or nutrient reaches the site of action  
Toxicity                                  Altered absorption  
Toxicity                                  Pre–systemic metabolism  
Toxicity                                  Hepatic metabolism |
| **Pharmacodynamic** | Loss of drug activity | Occurs at site of action  
Toxicity                                  Binding sites or receptors are involved |
| **Pharmacological** | Inability to provide EN therapy because of adverse effects | Extension of a drug normal pharmacological actions |
Known Drug–Nutrient Interactions
Phenytoin

- Liquid preparation is preferred for delivery through a tube.
- Phenytoin absorption reduced by up to 70% when combined with enteral feeds (Bauer, 1982).
  - Possible MOI: Phenytoin adhering to the tube; Phenytoin binding to certain components of EN such as proteins and calcium salts.

Interventions:
- Stopping EN for 2 hours before and after phenytoin administration then flushing the tube with 60mL water after drug delivery (Bauer, 1982).
- Withholding the enteral feedings for slightly shorter time period 1 hour before and after phenytoin administration with appropriate irrigation in between to ensure drug delivery and to maintain tube patency; phenytoin also given twice daily rather more often if possible to minimize amount of times feedings are withheld.
- Close monitoring of serum concentration.
Decreased absorption of suspension
Possible MOI: Adhere to actual feeding tube
Intervention:
  - Dilute suspension with an equal volume of sterile water or NSS before administration via enteral tube
  - Close monitoring of serum concentration
Warfarin resistance occurs in patients receiving EN.

Possible MOI:
- high amounts of Vitamin K in EN formulations
- Warfarin is highly protein bound therefore it may bind to the protein component of the EN formulation thus reducing bioavailability and interfering its anticoagulant effect

Intervention:
- Monitor PT or INR when warfarin is initiated
- Dose may be increased or switching to another anticoagulant may be necessary such as LMWH
- Continuous EN may be held for at least 1 hour before and after warfarin administration
- During transition from EN to oral feeding, reduction of warfarin dosage may be necessary
Bioavailability of drugs from this class may be reduced

Possible MOI
- Binding with multivalent cations such as calcium, magnesium, aluminum, iron

Studies on individual drugs
- Ciprofloxacin loss was the greatest followed by levofloxacin and ofloxacin (Wright et al, 2000)
- Ciprofloxacin absorption decreased significantly more then ofloxacin (Mueller et al, 1994)
- Moxifloxacin was not affected by concurrent EN (Burkhardt et al, 2005)
- Ciprofloxacin had greater reduction in both peak concentration and bioavailability when administered by jejustomy tubes versus gastrostomy tubes because the drug is primarily absorbed in the duodenum (Healy et al, 1996)

Intervention
- Do not give simultaneously
- Hold EN for at least 1 hours before and two hours after quinolone dosing (not applicable to moxifloxacin)
- Increase the dose of ciprofloxacin
- Ciprofloxacin suspension should not be given through feeding tube because it may adhere to the tube and cause occlusion
- Jejunal administration of ciprofloxacin must be avoided
Proton Pump Inhibitors

- Acid labile and inactivated by gastric acid and are specially formulated to maintain their integrity until delivery to the alkaline pH of the duodenum
- Omeprazole, esomeprazole, and lansoprazole – delayed-release capsules containing enteric-coated granule
- Pantoprazole and rabeprazole – delayed-release, enteric-coated tablets
When administered through large-bore NG or gastrostomy tubes, the capsule contents (omeprazole and lansoprazole) may be mixed with apple juice or orange juice, poured down the tube, and flushed with more juice.

Using acidic juices as the diluent allows the enteric-coated granules to remain intact until delivery to the small intestine, where the coating dissolves. Because of the potential for occlusion, this method of administration should not be used with small-bore feeding tubes.

Mixing the granules with water causes clumping and may lead to tube occlusion (Becwith et al, 2004; Nyfeller et al, 2005; Chun et al, 1996)
Proton Pump Inhibitors

- Esomeprazole granules, which are found in the delayed-release capsules and delayed-release oral suspension, should be mixed with water before delivery through the NG tube (Nexium package insert updated April 2007)

- Pantoprazole is available as an enteric-coated tablet and a new delayed-release oral suspension. This new suspension contains enteric-coated granules that are emptied into an oral syringe and mixed with apple juice for delivery via the NG tube (Protonix package insert updated Dec. 2007)
When administering omeprazole or lansoprazole capsules through small-bore jejunostomy or gastrostomy tubes, oral alkaline suspensions may be prepared to prevent drug degradation by raising gastric pH.

- Dissolve the intact enteric-coated granules in sodium bicarbonate 8.4% solution, which makes a simplified suspension.

(Becwith et al, 2004 and Phillips et al, 2001)
Practice Guidelines
Do not add medication directly to an enteral feeding formula. (B)
ASPEN Practice Recommendation #2

- Avoid mixing together medications intended for administration through enteral feeding tube given the risks for physical and chemical incompatibilities, tube obstruction, and altered therapeutic drug responses.(B)
Each medication should be administered separately through an appropriate access. (B)
- Liquid dosage forms should be used when available and if appropriate
- Only immediate-release solid dosage forms may be substituted
- Grind simple compressed tablets to a fine powder and mix with sterile water.
- Open hard gelatin capsules and mix powder with sterile water
- Soft gelatin capsules – aspirate/squeeze out and mix with 15 to 30mL water

Medications that SHOULD NOT BE CRUSHED
- Enteric-coated products
- Modified release drug products
- Cyototoxic tablets
Prior to administering the medication, stop feeding and flush the tube with at least 15mL water.

- Dilute the solid or liquid medication as appropriate and administer using a clean oral syringe (> 30mL in size).
- Flush tube again with at least 15mL water taking into account patient’s volume status.
- Repeat with the next medication (if appropriate)
- Flush the tube one final time with at least 15mL water
- Note: Dilution/flush should be less for pediatric doses (minimum 50:50 volume) and at least 5mL when fluid is not restricted.
Restart the feeding in a timely manner to avoid compromising nutrition status. Only hold the feeding by 30 minutes or more when separation is indicated to avoid altered drug bioavailability.
Use only oral/enteral syringes labeled with “for oral use only” to measure and administer medication through an enteral feeding tube.
ASPEN Practice Recommendation #7

- Consult with a pharmacist for patients who receive medications co-administered with EN.
Summary

- **A**void mixing EN and Medication
- **B**etter separate administration of patient’s multiple medications
- **C**onsider alternative route of administering the drug if possible
- **D**ilute oral drug dosage form with at least 15mL sterile water
- **E**nteral or oral syringes must be used to measure and administer the drug
- **F**lush prior to and after administration of a medication
- **G**o and consult your pharmacist
References:

- 2009 American Society for Parenteral and Enteral Nutrition (ASPEN) Enteral Nutrition Practice Recommendations
- Dickerson RN. Medication administration considerations for patients receiving enteral tube feedings. Hosp Pharm, 2004:39:84–89
Thank you!

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