

BARIATRIC SURGERY AND ITS EFFECT ON DRUG THERAPY

Jennifer Shieh, PharmD
PGY1 Pharmacy Practice Resident
Florida A&M University
January 23, 2010

OBJECTIVES

- To understand and discuss what bariatric surgery is
- To differentiate the various types of bariatric surgeries that exist
- To understand what pharmacokinetic parameters are affected by bariatric surgery
- To review the specific medications and dosage forms that are effected by bariatric surgery

BACKGROUND

- Morbid obesity affects 3-6 million in the U.S.
 - Resistant to behavioral changes, diet, medications
- Morbid obesity = BMI > 39 kg/m²
 - 6-12 fold increase in mortality
- Bariatric surgery has long lasting effects
 - Weight loss maintained over 5 years
 - Reduces caloric intake and absorption
 - Reserved for severely overweight with comorbid conditions

Sardo, P., and J. H. Walker. "Bariatric Surgery: Impact on Medication Management." *Hosp Pharm.* 43.113 (2008): 120.

TYPES OF BARIATRIC SURGERY

- Restrictive Procedures
 - Small pouch created at top of the stomach
 - Food passes through small hole at bottom of pouch
 - Limits quantity of food and prolongs satiety
- 1) Vertical-banded gastroplasty
- 2) Adjustable gastric banding

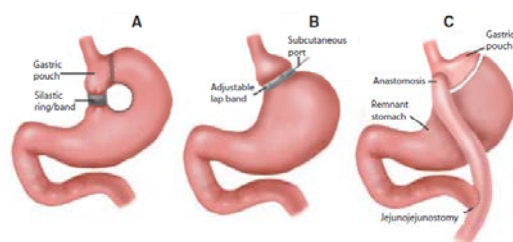
Sardo, P., and J. H. Walker. "Bariatric Surgery: Impact on Medication Management." *Hosp Pharm.* 43.113 (2008): 120.
Miller, A. D., and K. M. Smith. "Medication and Nutrient Administration Considerations After Bariatric Surgery." *Am J Health-Syst Pharm.* 63 (2006): 1852.

TYPES OF BARIATRIC SURGERY

- Combination restrictive-malabsorptive procedure
- 1) Biliopancreatic diversion
 - Nutritional deficiencies
- 2) Roux-en-Y gastric bypass
 - Most commonly performed procedure
 - Reduces how much stomach holds (50 mL) and reduces how much digestive tract absorbs

Sardo, P., and J. H. Walker. "Bariatric Surgery: Impact on Medication Management." *Hosp Pharm.* 43.113 (2008): 120.
Miller, A. D., and K. M. Smith. "Medication and Nutrient Administration Considerations After Bariatric Surgery." *Am J Health-Syst Pharm.* 63 (2006): 1852.

TYPES OF BARIATRIC SURGERY



Miller, A. D., and K. M. Smith. "Medication and Nutrient Administration Considerations After Bariatric Surgery." *Am J Health-Syst Pharm.* 63 (2006): 1852.

DRUG DISINTEGRATION

- First step for drug absorption
 - Rate limiting step of solid dosage forms
- Gastric mixing is reduced by restrictive bariatric surgery
- Administer liquid formulations or chew/crush solid dosage forms

Padwal, R., D. Brocks, and A. M. Sharma. "A Systematic Review of Drug Absorption Following Bariatric Surgery and its Theoretical Implications." *Obesity Reviews*. (2009).

Sardo, P., and J. H. Walker. "Bariatric Surgery: Impact on Medication Management." *Hosp Pharm*. 43:113 (2008): 120.

Examples of Oral Medications That Should not be Crushed

Generic	Brand	Comments
Alendronate	Fosamax	Esophageal irritation
Ciprofloxacin	Cipro	Unpleasant taste; available in suspension
Diltiazem	Cardizem CD, SR	Capsule may be opened and mixed with applesauce
Finasteride	Proscar, Propecia	Teratogenic if crushed or broken
Lithium	Eskalith CR, Lithobid	SR
Nifedipine	Procardia	Delays absorption
Omeprazole	Prilosec	DR; available in suspension
Pseudoephedrine	Sudafed 12 hour	SR; liquid form available
Tamulosin	Flomax	SR

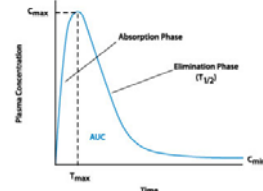
DRUG DISSOLUTION/SOLUBILITY

- Increased gastric pH in newly partitioned pouch
 - Pouch produces much less HCl
- Increased solubility of more basic drugs and decreased solubility of acidic drugs
- Higher pH may reduce disintegration of solid dosage forms-very drug specific
 - Rifampin, digoxin, ketoconazole, iron supplements
 - Calcium citrate does not require an acidic environment

Miller, A. D., and K. M. Smith. "Medication and Nutrient Administration Considerations After Bariatric Surgery." *Am J Health-Syst Pharm*. 63 (2006): 1852.
 Padwal, R., D. Brocks, and A. M. Sharma. "A Systematic Review of Drug Absorption Following Bariatric Surgery and its Theoretical Implications." *Obesity Reviews*. (2009).

REDUCED GASTRIC EMPTYING

- Reduced rate of drug absorption but not the overall magnitude of absorption
- AUC levels remain unchanged



Padwal, R., D. Brocks, and A. M. Sharma. "A Systematic Review of Drug Absorption Following Bariatric Surgery and its Theoretical Implications." *Obesity Reviews*. (2009).

DRUGS WITH SLOW DISSOLUTION PROPERTIES

- Avoid sustained release or enteric coated drugs
- Long absorptive drugs (SR, ER) are absorbed over 2-12 hours
 - Pass through the GI before absorption is complete
 - Substitute with immediate release drugs and increase the frequency
- Roux-en-Y bypass reduces the surface area
 - Villi and microvilli of small intestine (SI) have greater surface area than the long intestine
 - Bypass duodenum and jejunum
 - Digoxin absorption may be effected

Miller, A. D., and K. M. Smith. "Medication and Nutrient Administration Considerations After Bariatric Surgery." *Am J Health-Syst Pharm*. 63 (2006): 1852.
 Padwal, R., D. Brocks, and A. M. Sharma. "A Systematic Review of Drug Absorption Following Bariatric Surgery and its Theoretical Implications." *Obesity Reviews*. (2009).
 Malone, Margaret. "Altered Drug Disposition in Obesity and After Bariatric Surgery." *Nutr Clin Pract*. 18 (2003): 131.

Miller, A. D., and K. M. Smith. "Medication and Nutrient Administration Considerations After Bariatric Surgery." *Am J Health-Syst Pharm*. 63 (2006): 1852.

Table 1. Selected Agents with Potential for Decreased Absorption in Patients Who Have Undergone Bariatric Surgery

Drug	Possible Site(s) of Absorption	Management
Enalapril	Hydrolyzed to active form, enalaprilat, in stomach; absorbed in small intestine ¹	May exhibit decreased activity; consider other angiotensin-converting-enzyme inhibitors
Ketoconazole	Likely absorbed in stomach because acidic medium required for absorption ²	Absorption likely to be negligible; consider alternative agents ²
Lamotrigine	Likely stomach and proximal small intestine due to rapid and complete absorption ³	Monitor for and advise patients of decreased efficacy
Metformin	Slowly and incompletely absorbed in duodenum ⁴	Increased monitoring of blood glucose; drug requirements can decrease as weight loss occurs
Metoprolol tartrate	Absorbed rapidly and completely, indicating stomach and duodenum ⁵	Monitor blood pressure; medication requirements may decrease as weight loss occurs
Niacin	Primarily absorbed in duodenum ⁶	Administer with low-fat snack to maximize absorption
Olanzapine	Stomach ⁷	Monitor for decreased efficacy; switching to orally disintegrating tablet will not increase absorption (still absorbed in stomach)
Quetiapine fumarate	Exact location unknown, but likely stomach and duodenum due to rapid absorption ⁸	Monitor for decreased efficacy
Ramipril	Unknown; decreased absorption documented in patients with steatorrhea and malabsorption ⁹	Consider other agents; monitor blood pressure in the postoperative period; need for antihypertensives may decrease as weight loss occurs
Simvastatin	Absorption site unknown, but must be hydrolyzed to the active form in stomach ¹⁰	Consider other agents; monitor serum lipids
Zolpidem	Absorbed rapidly and completely; absorption affected by food ¹¹	Absorption time may increase, resulting in delay to effect; take on an empty stomach

HIGHLY LIPOPHILIC DRUGS

- Rely on availability of bile acids to enhance solubility
- Also undergo enterohepatic recirculation
 - Prolongs the elimination time
- Bypass of upper SI limits mixing of drugs with bile acids
- Lipophilic agents will have decreased absorption:
 - Cyclosporine, phenytoin, rifampin, thyroxine
 - Oral contraceptives undergo enterohepatic recirculation

Padwal, R., D. Brocks, and A. M. Sharma. "A Systematic Review of Drug Absorption Following Bariatric Surgery and its Theoretical Implications." *Obesity Reviews*. (2006).
Malone, Margaret. "Altered Drug Disposition in Obesity and After Bariatric Surgery." *Nutr Clin Pract*. 18 (2003): 131.

MEDICATION CONSIDERATIONS

- Avoid NSAIDs due to risk of ulcerations
 - Acidic properties of drug on GI mucosa
 - Inhibits prostaglandin synthesis
 - Exposes stomach to damage, erosions, ulcers
 - Options: COX-2 (celecoxib), APAP, opioids, tramadol
- Avoid oral bisphosphonates
 - GI ulceration due to reduced pouch size
 - Patients at risk of osteoporosis b/c of decreased calcium absorption
 - Options: calcitonin, teriparatide, raloxifene

Sardo, P., and J. H. Walker. "Bariatric Surgery: Impact on Medication Management." *Hosp Pharm*. 43.113 (2008): 120.
Miller, A. D., and K. M. Smith. "Medication and Nutrient Administration Considerations After Bariatric Surgery." *Am J Health-Syst Pharm*. 63 (2006): 1852.

MEDICATION CONSIDERATIONS

- Calcium absorbed through duodenum
 - Bypassed in RYBG surgery → Calcium deficiency
 - Calcium carbonate depends on acid to absorb
 - Substitute with calcium citrate instead
 - Recommend calcium 1200-1500 mg/day
- Life-long need for fat soluble vitamins due to fat malabsorption
 - Vitamins A, D, E, K

Sardo, P., and J. H. Walker. "Bariatric Surgery: Impact on Medication Management." *Hosp Pharm*. 43.113 (2008): 120.

MEDICATION CONSIDERATIONS

- Consume medications in crushed/liquid formulation for 3-8 weeks after surgery
- Consider other routes of administration
 - SQ, IV, rectal, vaginal, intranasal, transdermal
- Obesity linked to infertility
 - Consider nonhormonal, barrier contraception after weight loss
- Avoid medications that contribute to nausea, diarrhea, gastroesophageal reflux, gallstones, ulcers, obstruction

Sardo, P., and J. H. Walker. "Bariatric Surgery: Impact on Medication Management." *Hosp Pharm*. 43.113 (2008): 120.
Miller, A. D., and K. M. Smith. "Medication and Nutrient Administration Considerations After Bariatric Surgery." *Am J Health-Syst Pharm*. 63 (2006): 1852.

MEDICATION CONSIDERATIONS

- Minimize risk of dumping syndrome
 - Avoid sucrose, corn syrup, maltose, fructose, lactose, honey, mannitol
 - Avoid high-fat foods or drinking fluids with food
 - Symptoms: lightheadedness, palpitations, sweating, diarrhea
- Oral anticoagulants
 - Altered dietary intake and possible change in warfarin absorption

Sardo, P., and J. H. Walker. "Bariatric Surgery: Impact on Medication Management." *Hosp Pharm*. 43.113 (2008): 120.
Malone, Margaret. "Altered Drug Disposition in Obesity and After Bariatric Surgery." *Nutr Clin Pract*. 18 (2003): 131.
Parkes, Emmy. "Nutritional Management of Patients After Bariatric Surgery." *Am J Med Sci*. 331.4 (2006): 207-13.

QUESTIONS

1. Drug solubility and surface area for absorption are affected by gastric bypass procedures.
 - A. True
 - B. False
2. The small intestine provides the greatest surface area for drug absorption.
 - A. True
 - B. False
3. Patients with gastric bypass procedures are less prone to deficiencies of the fat-soluble vitamins (A,D,E,K) and calcium.
 - A. True
 - B. False

QUESTIONS???

