How Bariatric and Ostomy Surgeries Change Medication Strategies

Presented by
Jody Jacobson Wedret RPh, FASHP, FCSHP
Pharmacy Education Specialist/Clinical Professor
UCI Health

Objectives

• Identify physiologic changes made with these surgeries
• Describe changes in pharmacokinetics and pharmacodynamics that occur with bariatric and ostomy surgeries
• List best drug formulations to use in patients with limited GI tracts to assure efficacy

What is the GI tract

FUNCTIONS

Insert nutrients
Masticate/break down molecules
Absorb-cross into blood stream
Remove waste particles
Reabsorb excess waste
Eliminate waste

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**Bariatric surgical Roux en Y Gastric Bypass**


**Potential Benefits from surgery**

- Easy weight loss
- Reduction in glycemic lowering medications
- Reduction in blood pressure medication
- Lipid lowering dependent on patient
Results from surgery vary

- Caucasians see more weight loss compared to darker skinned people
- Older people have more complications
- Men with peripheral obesity (pears) do better than those with central obese (apples)
- Vertical banded procedures have less weight loss but greater safety than Roux-en-Y bypass


What nutritional supplements are recommended?

- Nutrients are often absorbed from the small intestines
- Once a day multivitamin
- Extensive detour around the duodenum may necessitate supplements of the following are needed:
  - COPPER
  - FOLATE
  - IRON
  - CALCIUM
  - ZINC

Pharmacokinetic considerations in bariatric surgery

- Absorption
  - May reduce stomach absorption
  - May affect time to peak
  - Does increase gastric pH (without PPI)
  - Does delay secretion of bile acids
  - Does decrease small intestinal surface area
Pharmacokinetic changes once absorbed

- Distribution
  - Volume of distribution changes
  - Lipid vs. hydrophilic ratios can change
- Metabolism
  - No changes to what is absorbed
- Elimination
  - Transit time and resorption may be reduced

Why the “may” statement regarding absorption?

- Many small studies done on specific drugs
- Bioavailability and Cmax can increase after surgery
- Proposed mechanisms:
  - Delayed gastric emptying
  - Decreased metabolism from intestinal CYP3A
  - Adaptation of GI tract post surgery
- Drugs where this was seen
  - Atorvastatin
  - Acetaminophen (one of two studies; in the other it was unchanged)
  - Metformin

Drugs where AUC and Cmax are reduced

- Drugs affected:
  - Sertraline
  - Tacrolimus
  - Sirolimus
  - Omeprazole
  - Oral midazolam
- Proposed mechanisms
  - Loss of absorptive surface
  - Bypassing influential CYP3A
Looking at one study of metoprolol and CR metoprolol

- **Design:**
  - Pharmacokinetic study of 200mg metoprolol immediate and sustained release 1 time dose each
  - 14 volunteers as own control before RYGB surgery and 6-8 months later
  - Measured AUC (0-24 hours after dose), Cmax and Tmax

<table>
<thead>
<tr>
<th>Patient demographics</th>
<th>Before RYGB</th>
<th>After RYGB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>110.4 (103.7, 118.2)</td>
<td>80.4 (74.6, 87.4)*</td>
</tr>
<tr>
<td>Body mass index (kg m^-2)</td>
<td>38.8 (37.0, 40.3)</td>
<td>28.3 (26.5, 29.9)*</td>
</tr>
<tr>
<td>Weight loss (%)</td>
<td>0</td>
<td>61.7 (54.3, 69.2)*</td>
</tr>
<tr>
<td>Fat percentage (%)</td>
<td>43.1 (38.8, 46.6)</td>
<td>32.7 (28.5, 37.0)*</td>
</tr>
</tbody>
</table>

* p < 0.05


Results of the study comparing metoprolol and CR metoprolol before and after surgery


Conjecture as to reasons for these results

- Highly soluble, highly permeable compound, passively diffused medication
- Decreased weight of patient may compensate for decreased absorption by reducing volume of distribution
- CYP2D6 and some CYP3A4 metabolism to active metabolite shouldn’t change with this surgery

Good old opioids in bariatric surgery

- Morphine absorbs in the jejunum
- Surgery gets it there faster
- Absorption is quicker for the immediate release
- Controlled release may not have sufficient transit time to sustain effect

Weight should be steadily declining

- Patients need to be at least 10% over ideal weight for surgical consideration
- Most are much more
- Weight based doses will need frequent adjustments
- “Steady state” weight may be 6-12 months from surgery

Summary of pharmacy related concerns in bariatric surgery

- Significant reduction in gut surface area
- Absorption is most significantly affected
- The site of absorption and the activity of the metabolites drive kinetic outcome
- Loss of intestinal length may reduce benefits of ER and CR dosage forms
Ostomy Effects

Are Medication recommendations after ostomy universal?

- **Colono-ostomies**
  - Gut function may be similar to normal bowels
- **Ileo-ostomies**
  - Mean limited absorption and shorter time to elimination
- **Urostomies**
  - Involve the urinary tract and have no intestinal interference on their own

Ideal drug dosage formulations for ileostomies

- Liquids
- Gelatin capsules
- Uncoated tablets
- Breakable capsules
- Patch therapy
Drug Formulations

- Immediate release capsule or tablet
- Liquid oral formulation either suspension or solution
- Topical
- Mucosal
- Injectable

Not good in many ostomy patients

- Extended/delayed release capsule or tablet
- Coated tablets

Coated tablets and extended release issues

- Don’t dissolve in the stomach
- Often not an issue with colonoscopies
- Big issue with ileostomies
- Not long enough gut exposure → insufficient absorption

- Why can’t you just break them open?
  - Harmful to stomach
  - Overdose—too much too soon

So, what should you tell patients who see a whole tablet in my bag?
Pharmacodynamic considerations in ostomies

Electrolytes and the ostomy

- Part of the bowel helps reabsorb fluids and electrolytes
- The following drugs can influence fluid and electrolyte balance
  - Diuretics—(i.e.) furosemide; hydrochlorothiazide, metolazone
  - Laxatives—increase movement, decrease reabsorption
  - Antibiotics—change flora—kill good AND bad bacteria—(i.e.) cephalaxin; ciprofloxacin
  - Corticosteroids—may increase sodium retention and fluid build up—(i.e.) prednisone; dexamethasone

So, what should you tell patients who must use a medication that interferes with electrolytes and fluids?

- Increase water intake
- Drink electrolyte supplements/sports drinks
  - (i.e.) Gatorade, All Sport, 10-K Thirst Quencher, Powerade
  - Be mindful of vitamin K containing supplements if on blood thinners
- Maintain salt intake
- Get blood levels drawn as recommended
Electrolyte Antacids

- Electrolytes
- Magnesium, aluminum and calcium are electrolytes
- Magnesium often causes diarrhea
- Aluminum often causes constipation
- Calcium can cause stones in susceptible people

- Take home point
- Magnesium/aluminum products are a good balance for most people if one needs an antacid

Other Antacids

- Histamine blockers—(i.e.) ranitidine, famotidine
- Proton pump inhibitors (i.e.) omeprazole, pantoprazole and lansoprazole

Usually don’t interfere with bowel movement

New evidence shows they can interfere with absorption of some medications and contribute to infections

For both, best to use only as needed, not routinely

What to counsel a patient complaining of gas

- It happens
- Simethicone in drops or tablets is great
- Avoid gas producing foods including soda, broccoli
- Avoid foods that the person specifically notices are ‘worse’
Pain management concerns

- Opioids
  - Will be constipating in many patients, not just people with ostomies
  - Does not ‘go away’ with time
  - Bulk laxatives (fiber products) may be best type
  - Avoid stimulant and osmotic laxatives in ileostomies
  - Stool softeners may also be helpful
- NSAIDs
  - Also pain relievers
  - May cause stomach bleeding

Other pain medications shouldn’t cause problems

- Nerve pain
  - Gabapentin
  - Pregabalin
  - Lidocaine
- Non-opioid
  - Acetaminophen
  - NSAIDs
- Anti-migraine medications
  - Sumatriptan*
  - Valproic acid
- Muscle relaxants
  - Cyclobenzaprine
- Antidepressant
  - Venlafaxine*
  - Duloxetine*

Anti-spasmodic and anti-cholinergic/histamine agents

- Anti-spasmodic
  - Used to relieve cramps
  - May reduce peristalsis-movement of food through the intestine
  - (i.e.) hyoscyamine; dicyclomine;
- Anticholinergic/antihistamines
  - Are internal drying agents
  - Diphenhydramine
Side effects of medications that may cause additional problems in patients with ostomies

- Antibiotics may lead to fungal infections and/or diarrhea
- Steroids and immunosuppressing drugs may also cause fungal infections
- Be observant of changes to skin
- With antibiotics, psyllium or other fibers increase bulk
- Remind patient to monitor for signs and symptoms of infections and irritations around stoma

Urostomy is special

- The bowel is intact; the urinary tract is not
- Kidney and urinary tract is where electrolytes and fluids are balanced normally
- Medication considerations
  - Calcium containing antacids (TUMs) may cause renal stones
  - Diuretics will increase fluid excretion and possibly electrolyte imbalance
  - Sulfas—as with all patients, important to drink lots of water

Important things to discuss with your patients

- Determine what procedure occurred
- Find out where the opening is
- For people with ileostomies, avoid extended release products
- Encourage hydration
Take home messages

- The changes from the surgery affect how the body responds to medication.
- Most of the changes have to do with absorption; how much gets into the body and how fast.
- Some drugs may have to be taken in smaller doses and at shorter intervals to get effects.
- Changes to the intestinal tract will require that most laxatives and some medications are avoided.
- Despite major anatomical changes, most patients can live relatively normal lives.

Thank You!

I’ll take questions

Speaker Contact Information:

Jody Jacobson Wedret RPh, FASHP, FCSHP
UCI Health
Phone: (714) 456 3789
Email: j3jacobs@uci.edu