



anti-diarrheals

by john dang

Objectives

- Discuss loperamide
- Discuss bismuth subsalicylate
- Look at studies comparing the two's efficacy.
- Compare and contrast the two OTC anti-diarrheal products and select a winner



Antidiarrheal agents

- loperamide hydrochloride
 - U.S. Proprietary Names
 - Imodium[®], Imodium A-D[®], Kaopectate[®]
- bismuth subsalicylate
 - U.S. Proprietary Names
 - Bismatrol[®], Pepto-Bismol[®], PMS-Bismuth Subsalsicylate[®]



Loperamide

- Anti-motility
 - Opiate class; second generation compound structrually and pharmacologically similar to diphenoxylate (Lomotil®)
 - Loperamide typically acts on the μ -opioid receptor.
 - “Loperamide are said to be gut-specific opiates because they have little CNS activity because of their rapid 1st pass metabolism. And does not easily pass the blood brain barrier.”¹

Loperamide

- It has been shown that loperamide has antisecretory activity against cholera toxin and E. coli heat stable toxin induced secretion.
- “The major side effects of opiates are CNS-induced sedation and addiction potential, actions that are minimal in loperamide, although they can occur even with this drug in infants and children...”¹

Loperamide

- “...possible worsening of infectious diarrhea due to gut stasis and presumably leading to increased bowel wall invasion by invasive infectious diarrheal organisms and prolonged excretion of pathogenic bacteria...”¹
 - Not intended for heavy bacterial-virulent related diarrhea. Unless used in combination with an antibiotic (Ciproflaxin + Lomotil)
 - Contraindicated in PTs Dx c dysentery

Loperamide

- Should only be used for mild to moderate diarrhea.
- Not indicated for use for children under six, unless MD approved
- Discontinue use diarrhea persists longer than 48 hours.
- Side effects
 - Rare cases²
 - Bloating, dizziness, drowsiness, rash, dry mouth.



Loperamide

- Usual Dosage
 - Not intended for children under the age of six
 - 6 to 8 yo
 - 2-mg po bid Do not exceed 4-mg/d
 - 9 to 11 yo
 - 2-mg po tid. Do not exceed 6-mg/d
 - 12 and over
 - 4-mg po after first loose BM, and 2-mg after each loose stool thereafter. Do not exceed 16-mg/d

Bismuth subsalicylate

- A mixture of trivalent bismuth and salicylate
- Due to the low pH of the stomach, bismuth subsalicylate reacts with HCl to form bismuth oxychloride and salicylic acid.
 - “99.1% of the bismuth is left to pass unaltered and unabsorbed into the feces.”¹

Bismuth subsalicylate

- May prevent infectious diarrhea through at least 4 possible mechanisms.
 1. Prevents the attachment or colonization of bacterial to the intestinal wall.
 2. Might act as a bacteriostatic or bacteriocidal to the invading bacteria
 3. Inactivates or prevents secretion of enterotoxins
 4. Might have antisecretory activity (controversial)

Bismuth subsalicylate

- “Bismuth has certain antimicrobial activity...bismuth salts are capable of binding to and killing bacteria, perhaps by interfering with bacterial ATP synthesis and/or loss of membrane integrity”¹
- One or two day courses of bismuth subsalicylate didn't have any significant effects on the normal microbial populations that normally reside in the intestines^{1,3,4}

Bismuth subsalicylate

- Bismuth subsalicylate is probably best used as a prophylactic measure against diarrhea. (prevention of Traveller's Diarrhea)
- This compound is also best effective against enterotoxigenic diarrheas, not useful in virulent related diarrheas.



Bismuth subsalicylate

- No significant side effects other than black stools caused by unabsorbed bismuth compound.
 - Not a big deal but may be mistaken as the melena of gastrointestinal bleeding.
- Can cause encephalopathy in instances in which patients reach blood levels 100-1000 μ g/L for prolonged periods
 - Large epidemic in the 1970s in Europe.
 - Today bismuth related encephalopathy due to renal insufficiency

Bismuth subsalicylate

- Usual Dosage
 - Under 3 yo
 - Dose based on weight
 - Under 13kg 2½-mL po PRN
 - Over 13kg 5-mL po PRN
 - 3 to 6 yo
 - 5-mL q½-1h PRN
 - 6 to 9 yo
 - 10-mL q½-1h PRN
 - 9 to 12 yo
 - 15-mL q½-1h PRN
 - Over 12 yo
 - 30-mL q½-1h PRN



Note: 15-mL = 262-mg bismuth subsalicylate ¹⁴

Studies

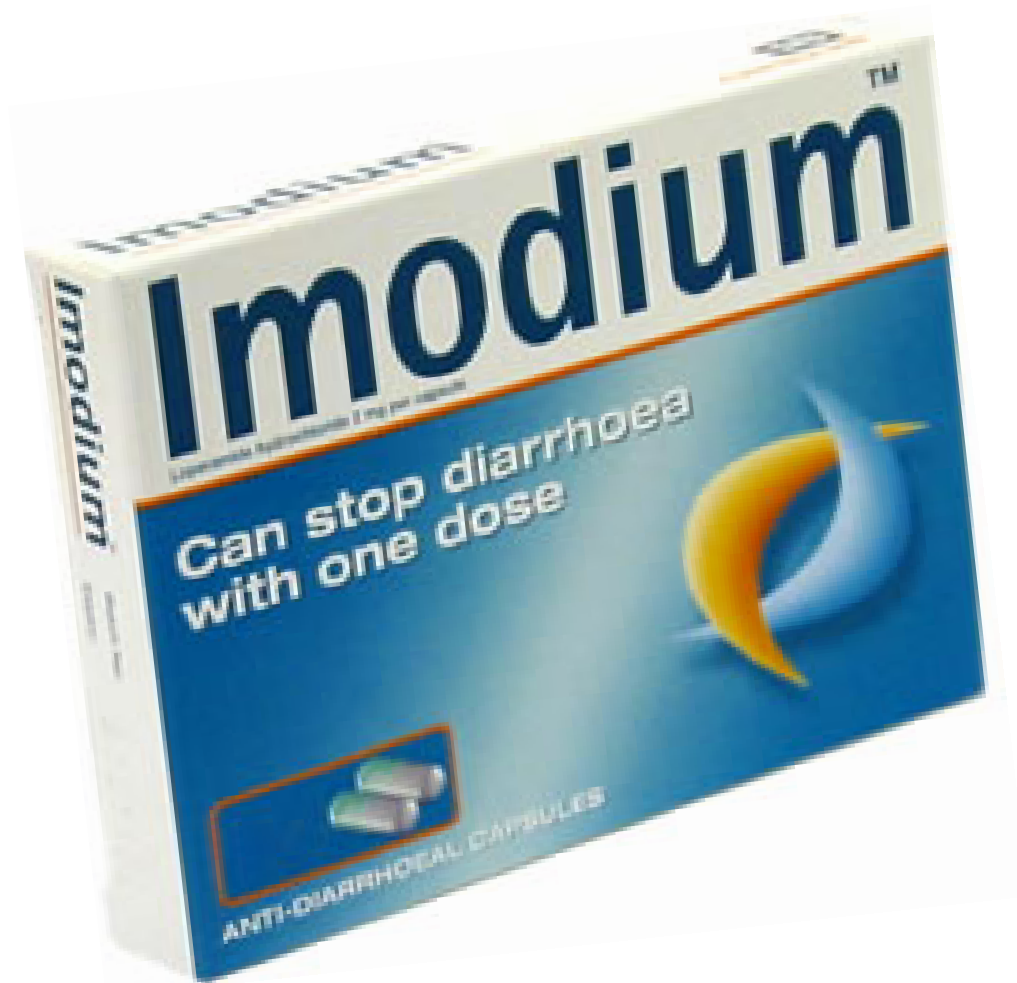
- In a randomized controlled, clinical trial done in 1990,

DuPont HL, et al. Comparative efficacy of loperamide hydrochloride and bismuth subsalicylate in the management of acute diarrhea. *Am J Med* 1990; 88(6A): 15S-19S.

“At [OTC] dosages, loperamide hydrochloride significantly reduced the average number of unformed bowel movements relative to bismuth subsalicylate... It was concluded that loperamide is effective at a daily limit of 8-mg for the treatment of acute nonspecific diarrhea and provides faster, more effective relief than bismuth subsalicylate.”³



We have a Winner!



References

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