GI pharma lec 5 antidiarrheals summary

Summary prepared by Dr:Ahmad Almohtaseb

Antibiotics-induced diarrhea

•Patient presents with a **bacterial infection** due to **overuse of antibiotics (clindamycin, cephalosporins, amoxicillin, etc.)** leading to **imbalance of normal microflora in the GI tract**.

This can cause overgrowth of Clostridium difficile (pseudomembranous colitis).

Management:-

• Rehydration and electrolytes correction.

• Stop the causative Antibiotic and switch to oral vancomycin.

• In severe cases → restore microbiota balance by giving patients unpasteurized yogurt لبن غير مبستر which contains large amounts of the harmless bacteria Lactobacillus acidophilus.

Management of acute diarrhea

1. **Replace fluids and electrolytes.(very important 1st step)**

2. Treat the underlying cause.

3. Antidiarrheal drugs.(might not be needed)

Antidiarrheals

Antimotility agents	Adsorbents	Agents That Modify Fluid And Electrolyte Transport	anticholinergics
Drugs: diphenoxylate and loperamide	: **Aluminum hydroxide and methylcellulose**	**bismuth subsalicylate**	**Atropine**
. • Chemistry: Analogues of **meperidine**(an opioid) **• Loperamide is a peripheral μ-opioid agonist** **• Mechanism of action**:- **activate presynaptic opioid receptors in the enteric nervous system → ↓ acetylcholine release → ↓ peristalsis.** **In normal doses these opioid agonist won't affect the CNS. But at high doses it will!!** **So we give other antidiarrheal drugs(eg. Atropine) in combination with antimotility agents so that we can use lower doses of antimotility agents** **• for the treatment of:-** **1. acute diarrhea** **2. chronic diarrhea** **3. traveler's diarrhea** **4. decrease the volume of discharge from ileostomies**  Contraindications:- **• Pediatric patients less than 2 years of age due to the risks of respiratory depression and serious cardiac adverse reactions.(due to opioid effect)** **• Patients with acute ulcerative colitis.** **• Patients with bacterial enterocolitis due to risk of toxic megacolon** **• Patients with pseudomembranous colitis** **Patients who have blood in stools**	• Mechanism of action:- **adsorbing يمتص intestinal toxins or microorganisms** and/or by **coating or protecting the intestinal mucosa.** **• Less effective than antimotility agents.** **• Can interfere with drug absorption.** **• Used for mild-to-moderate diarrhea**. **• Safe (They aren't absorbed by the body and are excreted with feces)** **• Cause some side effects including constipation.**	• Mechanism of action:- **Coating agent+ Decreases fluid secretion**. **• Used in prevention and treatments of traveler diarrhea.** • Adverse effects: **black tongue, dark stool**	**• Are not used alone in the treatment of diarrhea**. **• an oral tablet mixing Diphenoxylate (opioid derivative) and atropine (100:1) is called Co-phenotrope,** **This provides synergism and decreases side effects of opioids**. **• Anticholinergics block the parasympathetic system, which slows down peristalsis.** **This gives the intestines more time to absorb water in stool.** **• Sides effects: (ABCDs) Agitation, Blurred vision, Constipation, Dry mouth, Stasis of urine and sweat→urinary retention and hyperthermia**

Other diarrhea treatments: Probiotics

Probiotics **are non-pathogenic live microorganisms**. When ingested, probiotics can survive passage through the stomach and small bowel.

• **have preventive as well as curative effects on several types of diarrhea of different etiologies**.

• **Probiotics are effective for preventing Antibiotics-induced diarrhea**. Secondary analyses of higher dosages and certain species have shown **increased effectiveness.**

• **More research studies are needed that provide sufficient detail on interventions and outcomes** and are sufficiently powered to increase the evidence based on the effectiveness of probiotics **for the treatment of acute childhood diarrhea**.

Since there is no sufficient evidence for usage in any diarrhea→we use probiotics in certain situations only like antibiotic induced diarrhea

Traveler's diarrhea

• **Mainly Caused by Enterotoxigenic E.coli (ETEC),** but can be caused by other bacteria and viruses!!

• **Approach:-**

1.Rehydration.

2.Bismuth subsalicylate (mainly).

3.Loperamide.(if no contraindications for loperamide use)

The general rule is to avoid antimicrobials because ETEC diarrhea is self-limiting and not critical.

• **However, in special cases (elderly, severe diarrhea) we can give antimicrobials to terminate traveller's diarrhea faster: 1.Ciprofloxacin. 2.Cotrimoxazole**.

• **The use of probiotics for the prevention of TD is controversial**

Patient presents with diarrhea

• Usually, **most cases of acute diarrhea are caused by viruses and toxins and therefore are self-limiting, so our main goal is to rehydrate and replace electrolytes until diarrhea terminates**.

• **However, in cases of severe diarrhea or diarrhea that lasts for more than 2 days, we turn to antidiarrheals.**

If there are signs of bacterial gastroenteritis or IBD(blood in stool, fever,positive stool culture and fecal leukocytes etc…)

Use antibiotics and don't use antidiarrheals!!

• **In cases of chronic diarrhea that lasts for more than 2 weeks, we have to investigate the underlying cause.**

Irritable bowel syndrome (IBS)

Irritable bowel syndromeالقولون العصبي is defined as:-

recurrent abdominal pain on average, **at least one day per week in the last three months with two or more** of the following:

1. Related to defecation(either worsened or relieved)

2. Associated with a change in frequency of stool

3. Associated with a change in form of stool.

A 20-year-old woman presents to the clinic complaining of intermittent abdominal pain. She reports that the pain has been present for as long as she can remember and would improve after she defecates or when she is relaxed. It is especially worse now as she is feeling stressed because of final exams and her stools has also become watery of recent with more defecation episodes per day. Her past medical history is significant for an extensive gastrointestinal workup (e.g., fecal leukocytes, stool culture, fecal RBCs, and colonoscopy) with no abnormalities. A physical examination demonstrates an anxious patient with unremarkable findings

Types of IBS

Subtypes of IBS have been defined as follows:

1. **IBS with predominant constipation (IBS-C)** – Patient reports that abnormal bowel movements are usually constipation

2. **IBS with predominant diarrhea (IBS-D)** – Patient reports that abnormal bowel movements are usually diarrhea

3. **IBS with mixed bowel habits (IBS-M)** – Patient reports that abnormal bowel movements are usually both constipation and diarrhea

Management of IBS

• In patients with **mild and intermittent symptoms that do not impair quality of life**, we initially **recommend lifestyle and dietary modification.**

1. **Education and reassurance**

2. **Diet modification:**

• **Exclusion of gas-producing foods** e.g, beans, onions, celery, carrots, raisins, bananas, apricots, prunes, Brussels sprouts, wheat germ, pretzels, and bagels), alcohol, and caffeine.

• **Lactose avoidance :empiric trial of a lactose-free diet**

• **Gluten avoidance : non-celiac gluten sensitivity** ??

• **Fiber ? The role of fiber in patients with IBS is controversial**

• **Low FODMAP diet**: diet low in fermentable oligo-, di-, and monosaccharides and polyols (FODMAPs).

3. Increasing physical activity→reduction of stress

• In patients with **mild to moderate symptoms** **who fail to respond to initial management** **+ patients with moderate to severe symptoms that affect quality of life,**

we suggest pharmacologic therapy.

مهم جدا : ١-ممكن يجي السؤال انه تعطيك مريض معاه قولون عصبي IBS و constapation شو بتعطيه ؟ او معاه diarrhea شو بتعطيه ؟

Drugs used to treat IBS

٢- ممكن السؤال يكون على ال MOA-\\ ٣ - على ال contraindications

DRUG	INDICATION	MECHANISM OF ACTION	ADVERSE EFFECTS
Linaclotide	IBS-C*	Increases intestinal fluid secretion via increased cGMP	Diarrhea, abdominal pain, flatulence, and abdominal distention Do not use in children < 17 years old
Lubiprostone Lec 4	Women with IBS-C*	Chloride channel activator	Nausea and vomiting, dyspepsia, headache dizziness, and hypotension
Alosetron	Women with severe IBS-D	5-HT_3 antagonist	Constipation, nausea and vomiting, heartburn, ischemic colitis (rare)
Eluxadoline	IBS-D	μ-Opioid receptor agonist ↳ but, don't cause CNS manifestation	Constipation, abdominal pain, nausea, pancreatitis (rare) Possible risk of dependence and overdose
Rifaximin	Short-term use in IBS-D	Decreases bacterial load (structural analog of *rifampin*)	Nausea, fatique, headache, dizziness, peripheral edema, and risk of Clostridium difficile infection
Dicyclomine	IBS-C and IBS-D ↳ Mixed	Antimuscarinic; decreases GI spasms and motility	Anticholinergic effects such as drowsiness and dry mouth
Hyoscyamine	IBS-C and IBS-D	Antimuscarinic; decreases GI spasms and motility	Anticholinergic effects such as drowsiness and dry mouth Overdose may produce hallucinations, arrhythmias, and nausea and vomiting