PASSION ACADEMIC TEAM

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Sheet# 7

YU - MEDICINE

GASTROINTESTINAL SYSTEM

Lec. Title : Antidiarrheal Drugs .

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Diarrhea

لازم نعرف معناها قبل لا نعرف كيف نشخصها ونعالجها

–Is either increased frequency or increased looseness of stool

.abnormal frequent passage of loose stool (usually 3 or more loose watery stools in 24 hours) but we should know the normal bowel habit and compare to the normal in that patient in order diagnose it

Or

.abnormal passage of stools with increased frequency , fluidity , and weight , or with increased stools water excretion

Acute diarrhea:

-sudden onset in a previously healthy person
-less than 3 days
-self-limiting usually, because mostly viral diarrhea
-resolves without sequelae because it is mostly virus

Chronic diarrhea:

-longer than 14 days
-associated with recurring passage of diarrheal stools, fever, loss of appetite, nausea, vomiting, weight loss, and chronic weakness may be also headache

***why we are troubled from diarrhea?
-because of water and electrolytes loss that leads to these previous sequelae

Diarrhea of pathophysiology:

-decreased electrolyte and water absorption, because of irritation for instance
-increased secretion mucosa, so antisecretory is the treatment
-irritation of mucosal lining (by drugs or infection)

*in the matter of infection: the challenge is here would you give any patient with diarrhea antibiotics?

-you should not of course, firstly check for fever, tenesmus, the stool shape "if there is blood, mucus or not" and other sings of infection then decide and you should not surely give antibiotics if it is virus!
Examples for microorganisms cause diarrhea: shigella, ameba, E.coli (very pathogenic), salmonella.

*drugs because it may cause irritation

-stimulation of parasympathetic nervous system, if the problem is with increased motility, the treatment then is antispasmodic (anticholinergic)
-antibiotics that create an imbalance in normal intestinal flora, because among them there is bacteria regulate bowel habit, it is called lactobacillus, these bacteria when killed its function disappear and also give the space for superinfection like clostridium difficile to occur

Goals of treatment of diarrhea:

-manage the diet
-control the loss of fluid, electrolyte
-identify and treat the cause
-provide symptomatic relief
-sometimes diarrhea is a defense mechanism against pathogen

Treatment:

1_dieat management
2_treatment of fluid depletion, shock, and acidosis
3_drug therapy

Diet management:

-avoid dairy product
-stop solid hard food for 24 hours, hard food may be irritant
يعني مثال البطاطا ما ياكلها محمرة ناشفة بل يسلقها عشان تكون طرية وما تجرح الميوكوزا
-continue soft digestible food

Rehydration:

-not to stop diarrhea
-to restore and maintain hydration
-maintain electrolyte and PH balance

What is the role of oral rehydration (ORS)?
-just correct fluid, electrolyte and PH imbalance, some food has an alkaline action so loss of much protein and other alkaline foods cause acidity and rapid deep breath, then we should think that the diarrhea nay be the cause for patient complain from rapid deep breath as well as diarrhea

ORS:

-isotonic contain K**+, Na**+, **Cl**-, **Citrate**, and **Glucose** (important)
-use in mild cases of dehydration (loss of 5% of body weight)
-5 ml/kg/hr in children
*the over taking for these salts as ORS may induce vomiting because it is irritant, so your prescription must be in measure

IV rehydration used in these cases:

1_volume = 10% of body weight should be infused
2_in sever dehydration, or very weak
3_vomiting, it is very logic that we should not give ORS
-include: 1L solution of NaCl, KCl, NaHCo3 (because of acidosis) or 5% glucose

***الأرقام مش مهمة

Rationale for antibiotic therapy:

-limited rule in the treatment of diarrhea???
Clinical notes:
-the general rule for giving antibiotic to treat diarrhea = watery diarrhea + mucus in stool + fever
-if watery without mucus, do not give antibiotics, just give rehydration

-blood with stool is not mandatory, the mucus is mandatory to give antibiotics

.two types of diarrhea are caused by pathogens:

1-watery diarrhea without mucus with no fever: rota virus

.ORS is the therapy not antimicrobial

2-watery diarrhea with mucus or / and blood: shigella, C

.need antimicrobial

1_salmonella:

-ciprofloxacin, azithromycin, or IV ceftriaxone (5_7 days) (drugs of choice)

2_cholera:

-tetracycline and cotrimoxazole

3_clostridium difficile:

-metronidazole and vancomycin

4_ameabiasis:

- metronidazole (for intestinal or extraintestinal) or diloxanide furoate (if cysts present in in the stool only without trophozoite) but it is Ok, metronidazole (flagyl) is mostly effective in ameba cases

5_shigella enteritis:

-bloody and mucus stool

-treated with fluoroquinolone: ciprofloxacin or norfloxacin, cotrimoxazole is alternative

6_enteropathogenic Escherichia coli (EPEC):

-cotrimoxazole or fluoroquinolone

*to be clear, should we give antibiotics in any case of watery diarrhea?

Antidiarrheals: adsorbents

بتغلف بالجدار وبتلقط البكتيريا و السموم اللي بدها تعمل مصايب وتنزل بها في الstool

-coat the walls of the GI tract

-bind to the causative bacteria or toxic, which is then eliminated through the stool

-less effective than antimotility agents and they can interfere with the absorption of other drugs:

Bismuth subsalicylate (pepto-bismol), kaolin-pectin, activated charcoal, **attapulgite** (kaopectate)

NOTES:

*bismuth subsalicylate is the hero of GI because it is antiulcer, antimetric, adsorbent and antisecretory

*attapulgite is preparation from kaolin + pectin

*adsorbent is bought in form of sachets in market

natural adsorbent =لبن + حمض

Antidiarrheal: antisecretory

Octreotide:

-it is synthetic somatostatin analog that is growth hormone antagonist and act against serotonin

-highly effective in relieving diarrhea of carcinoid syndrome, which release serotonin that in turn increase the motility and mucus secretion

-given SC or in an IV infusion

Bismuth subsalicylate:

-used for traveler diarrhea (drug of choice)

-MOA: decrease chloride and fluid secretion in the bowel

-its action may be due to its salicylate component as well as its coating action

-suspension: 60ml 6hourly

Antidiarrheal: anticholinergics

-decrease intestinal muscle **tone** and **peristalsis** of GI tract

-result: slowing the movement of fecal matter through the GI tract, facilitate water absorption

-example: belladonna alkaloids (donnatal), atropine

-atropine extracted from belladonna plant

Antidiarrhea: antimotility

Opiates:

-antimotility that lessen peristalsis

NOTES:

-antispasmodic: decrease the tone "contraction"

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-antimotility: decrease peristalsis

#surely, we would not prescribe morphine for diarrhea but morphine analogs that do not cause addiction

##morphine and its analogs with antimotility action but increase the tone means it is spasmodic

###morphine has a congener (brother) that he is called meperidine, both of them cause addiction, but meperidine in turn has 2 sons:

Loperamide and diphenoxylate (these sons are meperidine-like drugs) and these do not cause addiction

-decrease bowel motility and relieve rectal spasm

-decrease transit time through the bowel, allowing more time for water and electrolytes to be absorbed

-example: paregoric (anhydrous morphine) opium tincture, codeine, **loperamide**, diphenoxylate + atropine (Lomotil) 5mg first followed by 2.5mg every 6hours

#to avoid colic resulting from morphine analogs, we give atropine that is antispasmodic in preparation called Lomotil diphenoxylate + atropine = (**Lomotil**) used also for traveler diarrhea

##**paregonic** (anhydrous morphine), another opiate drug

.the utility of antimotility drugs in diarrhea is limited to:

-non-infective diarrhea

-traveler diarrhea

-idiopathic diarrhea in AIDS

-in chronic diarrhea of **mild** IBD at low doses

.antimotility drugs is contraindicated in:

-acute infective diarrhea?? Because they delay clearance of the pathogen from intestine, if shigella, EC, EH present the use of antimotility increase risk of systemic invasion