

ANTIDIARRHEAL AGENTS



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- **LECTURE OBJECTIVES**

INTRODUCTION OF DIARRHEA AND CONSTIPATION

PATHOPHYSIOLOGY

CAUSES

TREATMENT

SPECIFIC

NON SPECIFIC

Normal bowel movement :

an average healthy person has three bowel movements a day, to three times a week ,depending on the person diet.

Diarrhea:

dia means ‘**flow**’ and **rrhoia** means **through**,so termed as **flowing through**.

Diarrhea is defined as an increase in the volume of stool,or passage of loose unformed (watery) stools at least 3 times or more per day

(stool frequency(>3) ,stool consistency (watery), and stool mass (stool weight >200g/day)

Constipation:

Inability to completely evacuate the bowels or passing very hard stools is known as constipation or a frequency of less than 3 stools per week

Types:

Acute

sudden onset and lasts from 3 days to less than 2 weeks

Persistent

from 2 to 4 weeks

Chronic

lasts for more than 4 Weeks



Causes of Diarrhea

Causes of Acute Diarrhea

- **Infections:** >90 percent
- Bacterial
- Viral
- Protozoal
- **Drug induced**
- **Toxic ingestions**
- **ischemia**



Cause of Chronic Diarrhea

Tumors

Metabolic disorders

Inflammatory

Malabsorption

Chronic infections



Pathophysiology of diarrhoea:

1 secretory

2 osmotic

3 inflammatory

4 dysmotility

5 malabsorption

Management:

specific therapy:

Anti microbial agents

Non specific therapy:

rehydration.

1.Oral and parenteral

2.Antidiarrhoeal Agents

SPECIFIC THERAPY

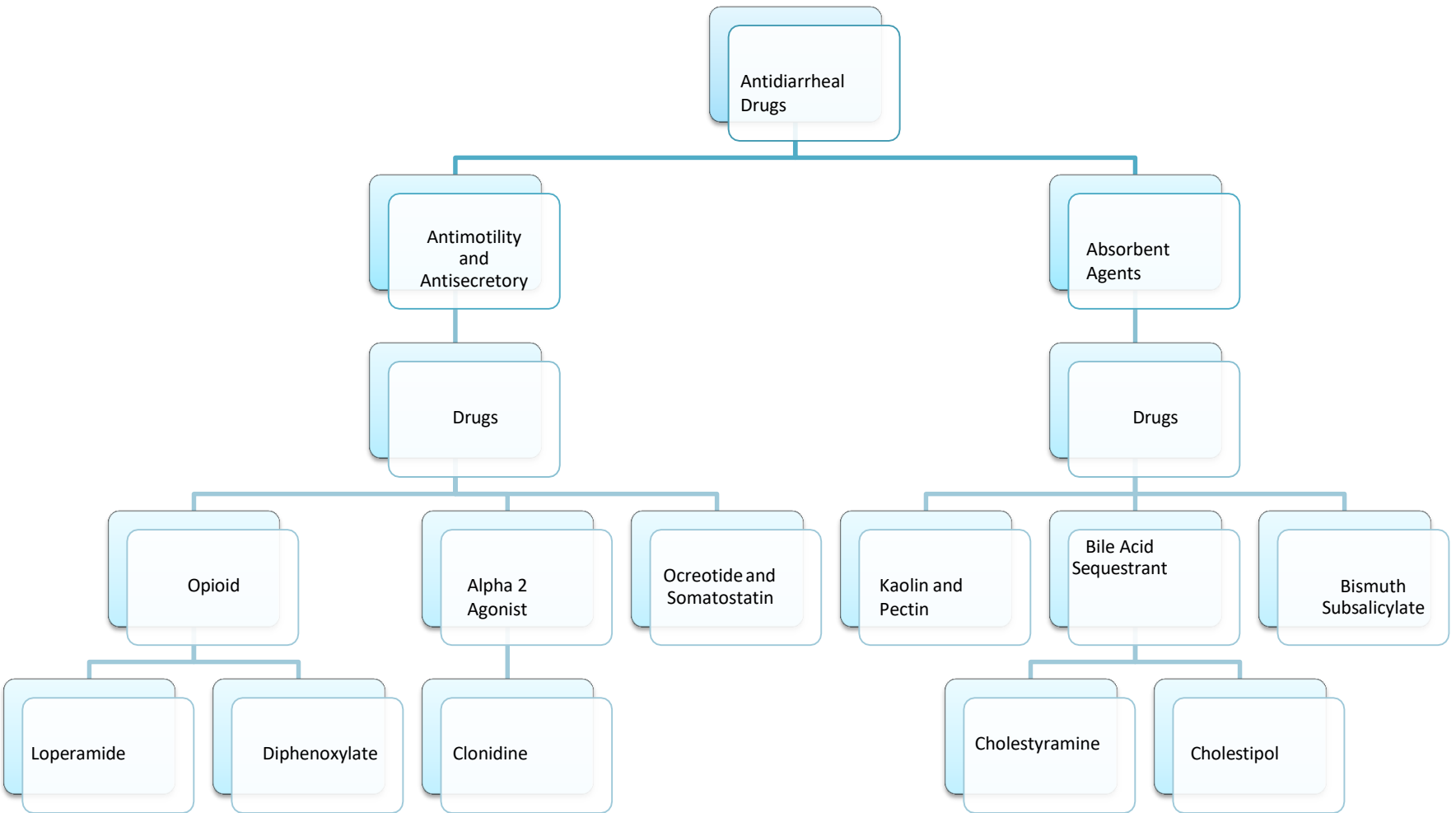
Antimicrobial agents

- Administration of Antimicrobial agents if The Diarrhea is of severe presentation with known microorganisms.
- Or Diarrhea persists for more than 3 days
- This will provide definitive treatment to the diarrhea

Fluid replacement therapy

- Administration of
 - Oral Rehydration Salt
- Is given depending on the severity of dehydration,
- This treatment is not curing the underlying causes of the diarrhea but rather prevent any worsening condition secondary to excessive loss of fluid and electrolytes





Antimotility and Antisecretory Agents

Opioid Agonists

Drugs	Mechanism of Action	Pharmacokinetics	Clinical Uses	Adverse Effects
Loperamide	<ul style="list-style-type: none"> • Opioid receptor agonist <ul style="list-style-type: none"> ○ Bind to μ receptor on the Myenteric Plexus of GIT • Stimulation of this receptor will lead to <ul style="list-style-type: none"> ○ Decrease the tone of longitudinal smooth muscle cells <ul style="list-style-type: none"> ▪ Increase transit time ○ Increase the tone of circular smooth muscle cells <ul style="list-style-type: none"> ▪ Increase the time for and capacity of intestine to absorb water ○ Inhibition of Gastrocolic reflex • All and all, it reduces GIT motility and increase transit Time 	<p>Absorption</p> <ul style="list-style-type: none"> • Poorly absorbed orally <p>Distribution</p> <ul style="list-style-type: none"> • Does not cross the BBB unless in a very high dose, therefore doesn't lead to Opioid dependency • 97% bound to plasma protein <p>Metabolism</p> <ul style="list-style-type: none"> • Hepatic metabolism <p>Excretion</p> <ul style="list-style-type: none"> • Urine • Bile 	<ul style="list-style-type: none"> • Travellers diarrhea • Chronic diarrhea 	<ul style="list-style-type: none"> • Abdominal pain • Bloating • Nausea • Vomiting • Constipation <p>Drug drug Reaction</p> <ul style="list-style-type: none"> • If admin together with <ul style="list-style-type: none"> ○ Quinidine ○ Omeprazole ○ Ritonavir • These are all CYP450 inhibitors which may elevate the plasma level of Loperamide to as high as 3 folds • These drugs enable Loperamide to pass the BBB and lead to sedative effects of Opioid agonists
			<p style="text-align: center;">Contraindication</p> <ul style="list-style-type: none"> • Children less in 2 years of age <ul style="list-style-type: none"> ○ Risk of fatal Paralytic Ileus • Diarrhea associated with organism that may penetrate the gut wall <ul style="list-style-type: none"> ○ E. coli ○ Salmonella • Symptomatic Pseudomembranous Colitis <ul style="list-style-type: none"> ○ Risk of toxin retention ○ Precipitate Toxic Megacolon • Hepatic failure <ul style="list-style-type: none"> ○ Precipitate Hepatic Encephalopathy 	
Diphenoxylate		<p>Absorption</p> <ul style="list-style-type: none"> • Good upon oral admin <p>Distribution</p> <ul style="list-style-type: none"> • Active metabolite Difenoxin may pass the BBB <p>Metabolism</p> <ul style="list-style-type: none"> • Hepatic <p>Excretion</p> <ul style="list-style-type: none"> • Urine • Bile 		

Antimotility and Antisecretory Agents

Drugs	Mechanism of Action	Pharmacokinetics	Clinical Uses	Adverse Effects
<p>Alpha 2 Agonists</p> <ul style="list-style-type: none"> Clonidine 	<ul style="list-style-type: none"> Binds to presynaptic Alpha 2 Adrenergic receptor It leads to reduction in the release of Neurotransmitters by inhibition of Adenylate Cyclase Exerts its antidiarrheal effects through <ul style="list-style-type: none"> Reducing GIT motility by Increasing transit time Increase GIT capacity Absorption of electrolytes and fluid <ul style="list-style-type: none"> Reducing secretion of fluid 	<p>Absorption</p> <ul style="list-style-type: none"> Good upon oral admin <p>Distribution</p> <ul style="list-style-type: none"> Plasma protein bound <p>Metabolism</p> <ul style="list-style-type: none"> Hepatic <p>Excretion</p> <ul style="list-style-type: none"> Urine 	<ul style="list-style-type: none"> Diarrhea in Diabetic patient Diarrhea due to withdrawal of Opioid 	<ul style="list-style-type: none"> Rebound hypertension Depression
<p>Octreotide and Somatostatin</p> <ul style="list-style-type: none"> Octreotide is a synthetic analogue for Somatostatin Octreotide has 400-500 more potency compared to Somatostatin 	<ul style="list-style-type: none"> Resembles the activity of Somatostatin Inhibits the release of various hormones <ul style="list-style-type: none"> GIT hormones <ul style="list-style-type: none"> Gastrin CCK-PZ Secretin Pancreatic Polypeptide Vasoactive Intestinal Peptide <ul style="list-style-type: none"> Other Hormones <ul style="list-style-type: none"> Insulin Glucagon TSH Growth Hormone Reduces fluid and electrolyte secretion from the Intestine <ul style="list-style-type: none"> Reduces GIT motility Vasoconstriction in the blood vessels 	<p>Absorption</p> <ul style="list-style-type: none"> Complete absorption after S/C admin <p>Distribution</p> <ul style="list-style-type: none"> Distributed across body compartment <p>Metabolism</p> <ul style="list-style-type: none"> Hepatic <p>Excretion</p> <ul style="list-style-type: none"> Urine 	<ul style="list-style-type: none"> Secretory diarrhea due to <ul style="list-style-type: none"> Hormone secreting tumor of Pancreas or Intestine Chemotherapy HIV Diabetes Mellitus 	<ul style="list-style-type: none"> Hypothyroidism Hypo/hyperglycaemia Reduce Insulin release QT prolongation Gallstones formation Bradycardia

Absorbent Agents

Drugs	Mechanism of Action	Clinical Uses	Adverse Effects
<p>Bulk-Forming and Hydroscopic Agents</p> <ul style="list-style-type: none"> • Kaolin <ul style="list-style-type: none"> ○ Naturally occurring hydrated Magnesium Aluminum Silicate • Pectin <ul style="list-style-type: none"> ○ Indigestible carbohydrate derived from apples. 	<ul style="list-style-type: none"> • May work as gels to modify stool texture and viscosity • Produce a perception of decreased stool fluidity • May bind bacterial toxins especially Enterotoxin • May bind to bile salts 	<ul style="list-style-type: none"> • Symptomatic relieve of <ul style="list-style-type: none"> ○ Acute diarrhea ○ Chronic diarrhea 	<ul style="list-style-type: none"> • Interfere with many oral drugs absorption in the GIT
<p>Bile Acids Sequestrants</p> <ul style="list-style-type: none"> • Cholestyramine • Cholestipol 	<ul style="list-style-type: none"> • Bile salt binding in the intestine • Leading to increase in bulk of the stool • Make the stools less watery 	<ul style="list-style-type: none"> • Bile salt-induced diarrhea <ul style="list-style-type: none"> ○ In patients with resection of the distal ileum 	<ul style="list-style-type: none"> • Hypertriglyceridaemia • Constipation • Bloating • Flatulence • Heartburn • Diarrhea • Steatorrhea • Malabsorption of Vitamin K <ul style="list-style-type: none"> ○ Hypoprotrombinaemia • Gallstones formation
<p>Bismuth Subsalicylate</p>	<ul style="list-style-type: none"> • Retarding the expulsion of fluids into the digestive system by irritated tissues, by "coating" them. • Stimulation of absorption of fluids and electrolytes by the intestinal wall (antisecretory action) • Reducing inflammation/irritation of stomach and intestinal lining through inhibition of prostaglandin G/H Synthase 1/2 • Reduction in hypermotility of the stomach • Binding of toxins produced by E. coli • Bactericidal action 	<ul style="list-style-type: none"> • Prophylaxis for Traveller's diarrhea • Treatment of H. pylori infection 	<ul style="list-style-type: none"> • Dark stools (sometimes mistaken for melena) • Black staining of the tongue

Thank you