Treatment of dysentery and amoebiasis

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- Main text
- Male slide
- Female slide
- Important
- Dr, notes
- Extra info

EDITING FILE

Objectives

- To understand different causes of dysentery.
- To describe different classes of drugs used in treatment of both bacillary dysentery and amebic dysentery.
- To be able to describe actions, side effects of drugs for treating bacillary dysentery.
- To understand the pharmacokinetics, actions, clinical applications and side effects of antiamebic drugs.
- To be able to differentiate between types of antiamebic drugs;luminal amebicides, and tissue amebicides.

Dr. Ahmed Nour Eldin

Dr. Fouda Video: Metronidazole

Dysentery

Definition

Inflammatory disorder of the intestine, especially of the **colon**, that results in severe **diarrhea** containing **mucus** &/or blood in the feces with **fever** & abdominal **pain** caused by any kind of infection.

Causes

- Viral Infections
- Parasitic / Protozoal Infestation
  - Amebic Dysentery
    - **Entameba Histolytica (mainly)**
- Bacterial Infections
  - Bacillary Dysentery
    - **Shigella (mainly)**

Treatment

Maintain Fluid Intake

Life saving, **first** thing to do

- Oral rehydration therapy
- IV fluid therapy In severe cases

Antimicrobial Agents

Not given until stool analysis is done & etiological agent is specified.

Antidiarrheal Drugs

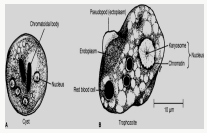
- loperamide
- Diphenoxylate

Contraindicated because they delay fecal excretion that can prolong fever.

Amoebiasis

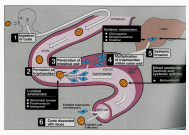
Definition

Protozoal infection of intestinal tract due to ingestion of foods or water contaminated with **cysts** **of Entameba Histolytica**.



Life Cycle

1. Cysts ingestion in contaminated food or water.
2. Liberation of trophozoites in the colon.
3. Invasion of intestinal wall.
4. Multiplication of trophozoites within colon wall.
5. Systemic invasion to other organs (liver, lungs, brain).
6. Cyst formation in rectum and excretion in feces.



Cysts (infective stage):
- Survive outside human body.
- When ingested, liberate trophozoites in intestinal lumen.

Trophozoites (invasive/non-infective stage):
- Multiply & feed on intestinal bacterial flora.
- May invade & ulcerate wall of large intestine or migrate to liver or other tissues.
- **In rectum:** transform to cysts → excreted in feces.

Clinical Presentation

- Varying degree of illness: no symptoms - mild diarrhea - severe dysentery:
  - **Asymptomatic amebiasis:** carriers (**passing cysts in stool**).
  - **Mild to moderate** intestinal disease: **colitis.** from here we begin the treatment
  - **Severe** intestinal infection: **amoebic dysentery** with inflammation & ulceration & diarrhea
  - **Ameboma: localized granulomatous lesion of colon** bleeding هنا يبدأ الـ
  - Hepatic abscess + other **extra-intestinal** diseases Rare, only if not treated

Treatment

Luminal Amebicides

Acts on: parasites in the bowel **lumen**.*"locally"*

Use: treatment of **asymptomatic** amebiasis (**carriers**) + eradicate cysts of *E. histolytica* after treatment of invasive disease.

- Diloxanide furoate
- Iodoquinol
- Antibiotics
  - Paromomycin
  - Tetracycline

Tissue or Systemic Amebicides

Act on: ameba in **tissues** (intestinal wall and/or other extra-intestinal tissues as liver - brain - lung).

Use: treatment of **systemic** form/**invasive** amebiasis (e.g. intestinal wall infection or liver abscesses).

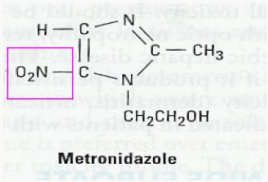
- Metronidazole/ tinidazole
- Emetine / dehydroemetine
- Chloroquine (**liver** only)

Amoebiasis: *Tissue/Systemic Amebicides*

Drug	Metronidazole (Flagyl®)

M.O.A.

- Inhibit **trophozoites** DNA replication.
- **Doesn't** eradicate cysts from intestine.



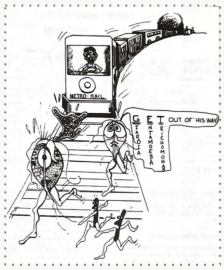
Metronidazole

P.K.

- **Administration:** orally or IV.
- **Absorption:** rapid & complete.
- **Distribution:** wide to all tissues & body fluids (CSF - saliva →metallic taste - milk →**#** in lactation).
- **Plasma half life: 8 hrs.**
- **Metabolism:** liver, by mixed function oxidase followed by glucuronidation (consider DDI).
- **Excretion:** urine.
- **Clearance:** decreased in **liver impairment**.

Uses

- **[Drug of choice]** treating all **invasive** amebic infections (tissue / intestinal & extraintestinal /extraluminal amebiasis).
  - **Followed by luminal amebicides ★**. To make sure no ameba exists.
- Giardiasis (Parasitic infection with Abdominal pain, diarrhea & weight loss)
- Drug of choice in Trichomoniasis an STD by parasite
- Anaerobic bacterial infections:
  - Pseudomembranous colitis (*Clostridium difficile*).
  - Peptic ulcer (*Helicobacter pylori*).



Metronidazole is usually misused: (بعض المرضى إذا جاهم ألم بالبطن يطلبونه من الصيدلية ويباع كمعقم أمعاء)

ADRs

- **GIT:** dry mouth - metallic taste - NVD[1] (preferred to be given with food to reduce)- oral thrush (**Moniliasis:** yeast infection).
- **CNS:** neurotoxicological effect - insomnia - dizziness - peripheral neuropathy - paresthesia - encephalopathy - convulsion (IV infusion, rare). due to ↑ distribution
- Dysuria - dark urine. (excreted in urine, not harmful but irritant)
- Neutropenia. (Not common, only in long term use)
- Disulfiram-like effect if taken with alcohol.

DDI

- **Enzyme inhibitors (*cimetidine - ketoconazole*):** increase metronidazole DoA.
- **Enzyme inducers (*phenytoin - phenobarbitone*):** decrease metronidazole DoA.
- Metronidazole **inhibits CYP-450 (*2C9 & 3A4*)** → increase anticoagulant effect of warfarin & lithium toxicity.
- **Alcohol:** blocks *aldehyde dehydrogenase* → **disulfiram-like effect** (nausea - vomiting - abdominal distress - flushing - headache - tachycardia - hyperventilation*)

*disulfiram (CNS remember) is a drug given to alcoholics to help them quit alcohol, basically it inhibit aldehyde dehydrogenase → ↑ acetaldehyde → develop these effects, Metronidazole has the same effect

#

- Pregnancy + breast feeding women
- Alcohol intake (due to disulfiram-like effect)
- CNS diseases (Crosses BBB)
- Severe renal/hepatic diseases (Need dose adjustment, it accumulates, need to check function regularly)

Amoebiasis: *Tissue/Systemic Amebicides*

Drug	Tinidazole	
M.O.A.	• Similar activity to metronidazole but better **potency**.	
P.K.	• **DOA:** 12-14 hrs **(longer)** ↓ Frequency of administration. • Simpler dosing regimen.	
ADRs	• **Better toxicity** profile than metronidazole.	
Drug	**Emetine**	**Dehydroemetine**
Intro.	• Alkaloid. • Derived from ipecac.	• Ipecac synthetic analog.
P.K.	• **Administration:** preferably SC, could be IM (**NEVER** I.V.) Because it's CVS toxic • **Absorption:** erratic/irregular oral absorption. • **Plasma half life:** 5 days (long). • **Metabolism + Excretion:** slowly via kidney → **cumulative** effect: builds up/accumulates in the body. • Should not be used for more than 10 days (usually/only 3-5 days).	
Uses	• Tissue trophozoites of E. histolytica (*irreversible* block of protein synthesis). • Intestinal wall infections • **Amoebic liver abscess** • Severe forms of amebiasis (acute amoebic dysentery). ○ Dehydroemetine is prefered (less toxic, 3-5 days). Metronidazole>dehydroemetine>emetine	
ADRs	• Major toxicity concerns → almost completely replaced by *metronidazole*. • **Toxicity:** dehydroemetine < emetine. • **GIT:** NVD • **Serious toxicities:** cardiotoxicity. • **CVS:** hypotension - cardiac **arrhythmias** - heart failure.	
#	• Pregnancy • Cardiac/renal disease • Young children	
Drug	**Chloroquine**	
Uses	• Anti-malarial drug • **Amebic liver diseases** with *metronidazole / dehydroemetine*	
ADRs	• Pruritus (*common*). itching • **GIT:** NV - abdominal pain. • Anorexia. • Blurring of vision. • Hemolysis (G6PD deficient) because it ↓ Glutathione (Antioxidant) → oxidative effect → hemolysis of RBCs	

Amoebiasis: *Luminal Amebicides*

Drug	Diloxanide Furoate	Paromomycin Sulphate
Intro.	• Ester of diloxanide + furoic acid.	• Aminoglycoside antibiotic.
M.O.A.	• Unknown. • Direct amoebicidal action against luminal forms. • Not active against trophozoites in intestinal wall or extra-intestinal tissues.	• Effective only against luminal forms of ameba. • **Direct amebicidal action:** causes leakage by its action on cell membrane of parasite. • **Indirect:** killing of bacterial flora essential for proliferation of pathogenic amoebae. • Inhibit protein synthesis

P.K.	• **Administration:** orally.
	• **In the intestine:** splits liberating diloxanide (Active amoebicidal ingredient)
	• **Absorption:**
	  ○ Unabsorbed → amoebicidal agent.
	  ○ Absorbed → excreted in urine.
		• **Administration:** orally.
		• **Absorption:** not significantly absorbed from GIT (small amount absorbed).
		• **Excretion:** unchanged in urine → may accumulate with **renal insufficiency.**

Uses	• **[Drug of choice]** treating all **asymptomatic** intestinal infections (*cysts* ***carriers/luminal amoebiasis***). • **Eradicate cysts** of *E. histolytica* ★ **after treatment of invasive** disease.	• Chronic amebiasis to eliminate cysts (in cysts passers). • Eradicate cysts of *E. histolytica* after treatment of invasive disease.
ADRs	• **GIT:** Flatulence - NV - abdominal cramps.	• **GIT:** distress - D.
#	• Pregnancy *(most of the drug crosses the placenta)* • Children <2 years.	***Precautions*** • Severe renal disease: accumulate & renal toxicity. • GIT ulceration patients.

Drug	**Iodoquinol** you can tell it has iodine from its name (iodo..)		
M.O.A.	• Unknown, effective against the luminal forms of amebiasis 		
P.K.	• **Administration:** orally.	• **Absorption:** poor.	• **Excretion:** feces.
Uses	• **Asymptomatic** amebiasis. *"Second choice after Diloxanide Furoate"*		
ADRs	• **GIT:** NVD (**Discontinue** if produces persistent diarrhea). • **Peripheral neuropathy** including optic neuritis (**caution** in optic neuropathy patients)could lead to pain in the eye & temporary vision loss → must be stopped • Enlargement of thyroid gland (**caution** in thyroid disease patients). *"because of Iodine release"* • Iodine sensitivity (**Discontinue** if produces signs of iodine toxicity: *dermatitis - urticaria - pruritus - fever*). • **Interference with thyroid function tests:** ↑ protein-bound serum iodine → ↓ measured ^{131}I uptake. Thyroid function tests should be taken either before the treatment of after few months (3 month gap) from stopping the treatment.		

Bacillary Dysentery (Shigellosis)

Antimicrobial therapy is typically administered for 5 days.

Reported resistance (*Ampicillin - Amoxicillin - Sulfonamides*) → not recommended as empirical therapy.

Treatment

Macrolides

- Azithromycin
  "used in children who have β-lactam allergy"

Fluoroquinolones

- Ciprofloxacin
- Ofloxacin

Cotrimoxazole

- TMP-SMX:
  TriMethoPrim - SulfaMethoXazole

In **traveller's** diarrhea

Beta-lactams

- Ampicillin
- Amoxicillin
- 3rd generation cephalosporins
  - Cefixime
  - Ceftriaxone

Drug	**Fluoroquinolones** (Ciprofloxacin)
M.O.A.	• Block bacterial **DNA synthesis** & growth (*DNA gyrase & topoisomerases*).
Spectrum	• Variety of gram positive & negative bacteria.
Uses	• **[First-Line Treatment]** of shigellosis. • **Bacterial diarrhea:** [shigella - salmonella - E. coli] • **Infections:** UTI - RTI - Soft tissues, bones, & joint infections.
ADRs	• **Arthropathy:** damage of growing cartilage in children → **#** in children & pregnancy. • **GIT:** NVD. • **CVS:** prolonged QT interval (*not significant*) but may cause torsades de pointes & arrhythmia • **CNS:** headache - dizziness. • **Toxicity:** phototoxicity - liver toxicity.
DDI	• Should NOT be combined with antacids, divalent cations → bind to drug → ↓its absorption → efficacy
#	• Pregnancy - nursing mother • Children • Epilepsy • Arrhythmias
Drugc	**3rd Generation Cephalosporins** (Cefixime - Ceftriaxone)
M.O.A.	• Interfere with synthesis of **peptidoglycan** (major structural component of bacterial cell wall).

P.K.	• **Administration (safe & effective):**
	  ○ Cefixime: oral.
	  ○ Ceftriaxone: parenteral.

Uses	• **[Second-Line Treatment]** of shigellosis. • Children and **pregnant** (then azithromycin). • Patient allergic to sulfonamides (then azithromycin).

Summary

Amebiasis	Treatment
Asymptomatic dysentery "cyst carriers"	• **Luminal amebicides:** Diloxanide or iodoquinol or Paromomycin
Amebic colitis **Dysentery ameboma** **Extra-intestinal disease**	• Metronidazole or tinidazole • followed by Luminal amebicides
Hepatic abscess	• Metronidazole or tinidazole or chloroquine or dehydroemetine

- Maintain fluid intake (*oral rehydration therapy / Intravenous fluid therapy*).
- **Asymptomatic** luminal amebiasis → luminal amebicides (diloxanide / iodoquinol / paromomycin).
- **Invasive** / intestinal amebiasis → metronidazole (*mainstay of therapy*) followed by luminal amebicides (*prevent relapse* by eradicating the cyst).
- **Hepatic** amebiasis → chloroquine - dehydroemetine (*CVS toxicity → not preferable*).
- Bacillary dysentery → ciprofloxacin (*drug of choice*).
- Bacillary dysentery in **children** & **pregnancy** → ceftriaxone / cefixime.
  Acute amoebic dysentery → dehydroemetine.

MCQ

1. a patient was tested for ameobiasis, a stool analysis revealed that there are cysts. The patient didn't complain of any symptoms, what is the best action to take?			
A. give him fluids	B. administer Metronidazole	C. administer Diloxanide furoate	D. Do nothing
2. Which of the following is contraindicated in patients with cardiovascular diseases?			
A. Iodoquinol	B. Metronidazole	C. Dehydroemetine	D. Chloroquine
3. Which of the following is contraindicated in patients with Neurological diseases?			
A. Iodoquinol	B. Metronidazole	C. Dehydroemetine	D. Chloroquine
4. Which of the following is used with caution in patients with thyroid diseases?			
A. Iodoquinol	B. Metronidazole	C. Dehydroemetine	D. Chloroquine
5. A patient came to the ER complaining of severe diarrhea, accompanied with blood and mucus. His temperature was high and a stool analysis was requested. What is the next step?			
A. administer IV fluids	B. administer antidiarrheal	C. Wait until stool analysis is done	D. administer Antibiotic
6. A child presented to the ER with abdominal pain, bloody diarrhea, fever. later he was diagnosed with bacillary dysentery. what is the drug of choice?			
A. amoxicillin	B. Azithromycin	C. Ceftriaxone	D. Ciprofloxacin

1:C ,2:C ,3:B ,4:A ,5:A ,6:C

SAQ

01

A pale 34 year old man presented in the ER with severe abdominal pain, bloody diarrheal episodes. he was diagnosed with bacillary dysentery,What is the drug of choice, its MOA, and ADRs?

Ciprofloxacin, slide 8

02

What are the side effects of metronidazole?

Slide 5

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