

Pharmacology Team

Chemotherapy of Tuberculosis

By :Prof. Azza El-Medany



Notes in Blue

المذكرة عبارة عن سلايدات د.عزة
بالإضافة إلى نوت التيم

429 Medicine

Maha Al-Balharith

Sarah Bin-Hussain

Reham Al-Henaki

Norhan Al-shamma'

Nourah Al-syefi

Designed By

Wejdan Al-Suwayyid

Types of TB:

1- typical TB by mycobacterial organism → هو اللي بنتكلم عنه

2- A typical TB → manifestation مختلف في العلاج treatment الـ

Site of infection:

Apical area of the lung

Renal

Growing end of the bone

Drugs of TB:

First line

Second line

أقل مدة للعلاج : ٦ شهور

=)

Tuberculosis

- Common sites of infections
- Apical areas of lung
- Renal parenchyma
- Growing ends of bones
- Where oxygen tension is high

Transmission

- Through inanimate objects
- Through air (air borne transmission)

Treatment Of Tuberculosis

- Tuberculosis remains the primary cause of death due to infectious disease.
- Periods of treatment (minimum 6 months)
- Drugs are divided into two groups:
- First line
- Second line

Antimycobacterial drugs:

- **First line of drugs:**

- Isoniazid (INH)
- Rifampin
- Ethambutol
- Streptomycin
- Pyrazinamide

INH and Rifampin is the most important drugs

لازم نستخدمهم في العلاج

قاعدة نطبقها في علاج الـ TB

Never use single drug when treating TB

Because mycobacterial organism has high resistance

Never use a single drug therapy

- Isoniazid –rifampin combination administered for 9 months will cure 95-98% of cases .
- Addition of pyrazinamide for this combination for the first 2 months allows total duration to be reduced to 6 months.

Isoniazid

- Bacteriostatic for resting bacilli.
 - Bactericidal for rapidly dividing bacilli.
 - Is effective against intracellular as well as extracellular bacilli

Bacteriostatic: inhibit growth → organism in resting case
Bacteriocidal: kill the micro organism → in active case

Mechanism Of Action

- Is a prodrug, activated by mycobacterial enzyme
- Inhibits synthesis of mycolic acid----
(component of mycobacterial cell wall).

Clinical uses

- Mycobacterial infections
- Latent tuberculosis in patients with positive tuberculin skin test

Latent: person has TB without clinical manifestation

- Prophylaxis against active TB in individuals who are in great risk .

Adverse effects

- ❖ Peripheral neuritis
- ❖ Optic neuritis & atrophy.
(Pyridoxine should be given)
- ❖ Allergic reactions
- ❖ systemic lupus erythematosus
- ❖ Hepatitis

Effect on the absorption of vit.B6(other name :pyridoxine)
That mean patient who take INH will suffering from a lack of vit B6 -> the most imp manifestation is neuritis (التهاب الاعصاب)
So we give the patient vit B6 to avoid neuritis

Drug Interactions of INH

- Inhibits the hepatic microsomal enzymes, cytochrome P450 .

Potent enzyme inhibitor: inhibit metabolite of other drugs, So we have to decrease the dose of other drugs to avoid the side effect

Rifampin

- Bactericidal
- Inhibits RNA synthesis.

Any drug that inhibit synthesis of DNA and RNA , and it is bacteriocidal--> irreversible inhibitor synthesis of RNA

Site of Action

- Intracellular bacilli
- Extracellular bacilli

Clinical uses

- Mycobacterial infections
- Prophylaxis of active tuberculosis.
- Treatment of serious staphylococcal infections.
- Meningitis by highly resistant penicillin pneumococci

Adverse effects

- Harmless red-orange discoloration of body secretions .
- Hepatitis
- Flu-like syndrome
- Hemolytic anemia

Drug Interactions

- Potent inducer of hepatic microsomal enzymes (cytochrome P450)

Enzyme inducer (عكس اللي قبل)
 -> increase metabolism of
 other drugs
 So we have to increase
 the dose of them =)

Ethambutol

- Bacteriostatic
- Inhibits mycobacterial arabinoglycan a component of mycobacterial cell wall

Site Of Action

- Intracellular & Extracellular bacilli

Clinical uses

- Treatment of tuberculosis in combination with other drugs.

Adverse effects

- Optic neuritis causing loss of visual acuity
- red-green color blindness.

(Relatively contraindicated in children under 5 years).

المريض لازم بين كل فترة وفرة

- Hyperuricemia **Increase uric acid level**

Pyrazinamide

- Prodrug.
- Bactericidal
- Mechanism of action is unknown .

Site Of Action

- Active against Intracellular Bacilli

Clinical uses

- Mycobacterial infections mainly in multidrug resistance cases.
- It is important in short –course (6 months) regimen.

- Prophylaxis of TB .

Ethambutol يؤخذ هو أو الـ isoniazid and rifampicin في أول شهرين من العلاج مع الـ
 isoniazid and rifampicin وباقي الاربعة شهور يأخذ الـ

Adverse effects

- Hepatotoxicity
- Hyperuricemia
- Drug fever & skin rash

Streptomycin

- Bactericidal
- Inhibitors of protein synthesis by binding to 30 S ribosomal subunits.
- Active mainly on extracellular bacilli

Clinical uses

- Severe , life-threatening form of T.B. as meningitis, disseminated disease.

Adverse Effects

- Ototoxicity
- Nephrotoxicity
- Neuromuscular block

Indication of 2nd line treatment

- Resistance to the drugs of 1st line.
- Failure of clinical response
- There is contraindication for first line drugs.
- Patient is not tolerating the drugs first line drugs.

or b/c of the side effect

2nd line ? .. ليش سميناها ..
 - 2nd line less potent than 1st line ,
 - side effect in 2nd line more serious than 1st line .
 - more effect in A typical T.B.

Ethionamide

يشبه INH

- Inhibits the synthesis of mycolic acid

INH : bacteriostatic and bactericidal but مثل الـ
 1- bacteriostatic : in low dose
 2- bactericidal : in high dose

Clinical uses

- As a secondary line agent.

Adverse Effects

Poorly tolerated
Because of :

- Severe gastric irritation &
- Neurological manifestations

أخطر بكثير من
INH
خاصة في
Neurological
manifestations
يسبب التشنجات
“convulsion”
العصبية
To reduced it
نعطي معه
Vit B6

Cycloserine

- Inhibitor of cell wall synthesis **bactericidal**
- The most serious side effects are peripheral neuropathy and CNS dysfunction.
- Pyridoxine should be given.
- Contraindicated in epileptic patients.

The most sever

مايعطى لمرضى الصرع

Fluoroquinolones (Ciprofloxacin & Levofloxacin)

- Effective against multidrug- resistant tuberculosis. **resistant** معناه اذا كانت
- Block DNA bacterial synthesis

مهمة : لأن لها organism كثيرة :

تأثير على
“gram⁽⁺⁾ .(-) “ Anaerobic , aerobic - typical . A typical
mycobacteria

Adverse effects

- Nausea , vomiting , diarrhea common
- Prolong QT interval = ventricle arrhythmia
- تكون خطورته مع المريض المصاب بـ M.I
- Damage growing cartilage (arthropathy)
مايعطى للي أعمارهم أقل من ١٨ عشان مايؤثر على النمو

In adult : rupture tendon

Rifabutin

- RNA inhibitor.
- Cross –resistance with rifampin is complete.

يعني لو صار resistance للـ rifampin
وحولنا للـ 2nd مانختار Rifabutin
لأنه لو قاوم الأول أكيد يقاوم الثاني ..

- Enzyme inducer for P450 (hepatic enzymes).
But less potent وهذا بينفعنا في الاستخدامات له ..
than rifampin

Clinical uses

- Effective in prevention & treatment of T.B. in AIDS patients.

يفضل عن الـ

Rifampin**In:**

- Viral infection
- First choice for AIDS patients

Adverse Effects مثل rifampin

- GIT intolerance
- flue- like syndrome
- Orange-red discoloration of body secretions.

Aminosalicylic Acid (PAS).

- Bacteriostatic = inhibit growth by Inhibits Folic acid synthesis.
- Folic acid ضروري للنمو

Clinical uses

- AS a second line agent is used in the treatment of pulmonary & other forms of tuberculosis. Extra – pulmonary “ brain ,liver ,spleen”

Adverse effects

- GIT upset (anorexia, nausea, diarrhea, epigastric pain).

عشان نحل المشكلة

-take it in meals or immediate after meals :**- Anti acidic** مضادات الحموضة منها بيكربونات الصوديوم

- Hypersensitivity reactions “allergy “
 - hematological change ... أخطر شئ ونحتاج وقتها نوقف العلاج ...
- Crystalluria = stone in urinary tract “ in bladder...etc

TB & Pregnancy

- Untreated TB represents a great risk to the pregnant woman & her fetus than the treatment itself.
- First line drugs are given for 9 months in normal doses
- Streptomycin is the last alternative in treatment
- ototoxicity ويمكن يولد الطفل أصم

TB & Breast Feeding

- It is not a contraindication to receive drugs , but caution is recommended

Children with T.B :

نفس الأدوية لكن تختلف الجرعة المعطاة

Except ethambutol
visual acuity لأنه يسبب
وصعب المتابعة مع الأطفال (=