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Review Article

Anti-Tubercular Agents: Overview

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ABSTRACT

During the last few years, the pharmacy profession has expand significantly in terms of professional services delivery and now has been recognized as an important profession in the multidisciplinary provision of health care. The main objectives of tuberculosis therapy are to cure the patients and to minimize the possibility of transmission of the bacillus to healthy subjects. Adverse effects of antituberculosis drugs or drug interactions (among antituberculosis drugs) can make it necessary to modify or discontinue treatment.

KEYWORDS

Bacteriocidal, Bacteriostatic, Neuritis, Tuberculosis

INTRODUCTION

Robert Koch in 1882, discovered tubercle bacillus thus the disease was referred as tuberculosis. It's a systematic disease commonly involves in respiratory system but affect other organs.

Tuberculosis is a disease caused by Mycobacterium tuberculae, a bacteria that is passed between peo ple through the air.The disease can be cured with proper drug therapy, but because the bacteria may become resistant to any single drug,combinations of antituberculosis drugs are used to treat tuberculosis (TB) are nor mally required for effective treatment. Atthe start of the 20th Century, tuberculosis was the most common ca use of **death** in the United States, but was lareglyeliminated with better living conditions. It is most common

in areas of crowding and poor ventilation, suich as crowdedurban areas and prisons. In some areas, the **AID S** epidemic has been accompanied by an increase in the prevalence oftuberculosis[1].

Some antituberculosis drugs also are used to treat or prevent other infections such as *Mycobacterium avium* complex (MAC),

DEFINATION OF TUBERCULOSIS: Tuberculosis is a chronic infectious disease which may caused by *Mycobacterium Tuberculosis* is called as tuberculosis[1].

TUBERCULOSIS CONSISTS OF[2]:

1) PRIMARY PULMONARY TUBERCULOSIS (PPT);
   - With primary tuberculosis the source of organism is exogeneous.
   - It occurs in individual who may loss their sensitivity for autoimmune system of body to *tubercule bacillus* & also may develops primary tuberculosis more than once.
2) SECONDARY PULMONARY TUBERCULOSIS (SPT);
   - It is also called as reactive tuberculosis.
   - It may follow shortly after primary pulmonary tuberculosis in which resistance of the body is decrease.
   - It is an exogeneous re-infection it is manly found in the apex of one or both the upper lobes of lungs.
3) MILLIARY TUBERCULOSIS (MT);
   - It is an extra- pulmonary form which results from progressive primary tuberculosis as well as secondary tuberculosis.
   - This is a lymphohaematogeneous disease which spread in later stages into systemic organ or isolated organ as liver ,kidney ,brain, pulmonary artery ,lymph nodes and bone cells etc.

DEFINATION OF ANTI-TUBERCULOSIS[2]:

Anti-tuberculosis may be defined as these are the pharmacological agent which when administer they use in treatment of tuberculosis (T.B)

CLASSIFICATION OF ANTI-TUBERCULAR DRUGS:

Classification of Anti-tubercular drug is based on their efficiency of low toxicity (safety). The agents are classified into two groups:

A) FIRST LINE AGENTS[3]:

1. BACTERIOSTATIC (These are the agent which stop the growth of bacteria or micro-organisms). Eg: Etambutol (E), Paraminosalicylic (PAS), Thiacetazone(T)
2. BACTERIOCIDAL: (These are the agent which are use to kill the bacteria or micro-organisms). Eg: Isoniazide(INH), Rifampicin(R), Streptomycin(S)

B) SECOND LINE AGENTS:

1. BACTERIOPSTATICS: Eg: Etionamide(Eth), Cycloserin(C)
2. BACTERIOSTATICS: Eg: Kenamycin(k), Cycloserin(C)

FIRST LINE AGENTS:

F= Field defects causing drug i.e. Ethambutol (E).

I= Isoniazid(I).

R= Rifampicin(R)

S=Streptomycin(S)

T= Twice a day given drugs i.e. Pyrazinamide.

(All the first line drugs are given once a day).

In general the FIRST line drugs used to treat- drug sensitivity T.B. are better tolerated than the SECOND line medication for drug resistant T.B.

Eg: Isoniazide, Rifampicin, Pyrazinamide, Ethambutol, Streptomycin

SECOND LINE AGENTS: These drugs have either low antitusercular efficacy or high toxicity or both used in special circumatances only.

Eg: Ethionamide,Cycloserin, Amikacin, Aminosalicylic acid

MECHANISM OF ACTION[3]:

- Interference with initiation complex of peptide formation.
- Misreading of code of m-RNA.
- Incorporation of incorrect Amino acid into the peptide chain.
- Resulting on non-functional or toxic protein.
- Inhibition of translocation.
- Break up of polysome into non functional monosomes.
- The activity occours simultaneously & overall effect is the lethal for the cell.

IDENTIFICATION TEST FOR TUBERCULOSIS:

TUBERCULIN OR MANTOUX TEST[4]

a. This Test is performed to find out whether any particular person had any previous tuberculosis infections or not.

b. Sufficient quantity of tuberculin solution (5 tuberculin units) is administered intradermaly into the skin of the left forearm.

c. The site of the Injection is examined after 72 hrs i.e. Three Days.

d. This Test is considered positive if there is swelling of at least 6-10mm in diameter at the site of Injections.

e. The Redness of the skin is no considerations.

f. Reactions less than 6 mm in diameter are considered negative and BCG Vaccination is therefore administered.
g. Preliminary tuberculin testing for new- born infants is unnecessary.

FIRST LINE DRUG:

1) ISONIAZID (INH)[5]

Isoniazid is one of the most important drug in the used in treatment of tuberculosis.(T.B)

It has been used since 1952.

The structure of isoniazid is simple.

It comprises a pyridine ring & a hydrazine group

The minimum inhibotry concentration of isoniazid for mycobacterium tuberculosis is 0.02-0.20.

MECHANISM OF ACTION OF ISONIAZID[1].

a. Isonizid is a prodrug and must be ACTIVATED BY THE *Mycobacterium Tuberculosis* catalase-PEROXIDASE ENZYME KatG;
b. The activation of isoniazid produces oxygen derived from free radicals (superoxide, Hydrogen peroxide)
c. Organic free radicals that inhibit the formation of MYCOIC ACID of the bacterial cell wall.
d. Which causing DNA damage & subsequently the death of the bacillus.
e. The most common mechanism of resistance to isoniazid consists of K at G Mutation.
f. Which decreases the activity of isoniazid & prevent the PRODRUG from being converted into its active metabolites.

PHARMACOKINETICS OF ISONIAZID:

- Isoniazid completely absorb orally& penetrate all the body tissues tubercular cavities, placenta mengis.
- Isoniazide is metabolized in liverthrough bacetylation by N-acetyltransferase which produces acetylisoniazid & isonicotinic acid.or
- It is extensively metabolized in liver most (important pathway being acetylation.
- Isoniazid is excreted by kidney in the form of urine.
- Fast acetylators
- (30-40%of Indians) t1/2 of INH 1 Hrs.
- Slow acetylators, (60-70% of Indians) t1/2 Of INH 3 hrs.
- The proportion of the fast & slow acetylators different in different part of the world.
- However acetylator s status do not matter.

- If INH taken orally or daily but biweekly regimers are less effective in fast acetylator.
- INH induced peripheral neuritis appears to be more common in slow *acetylatiors.*

PREPARATION OF ISONIAZID[3]:

- Isoniazid elixir (syrup).
- Isoniazid injections.
- Isoniazid & rifampicin tablets
- Isoniazid & Ethambutol tablet

TRADE NAME OF ISONIAZID:

- Ionex
- Rimpazid
- Isocadipas
- Cadizide

THERAPUTIC USES OF ISONIAZID[1]:

- Isoniazid use in treatment of pulmonary tuberculosis.
- Isoniazid also use in treatment of Extra- pulmonary Lesions including menengeal & Genito urinary infections.
- As isoniazid develops registance within a few weeks.
- It gives in combination with ethambutol or Rifampicin.

CONTRAINDICATIONS:

- It should be contraindicated in following conditions .
- Diabetes is not under control
- Habit of drinking too much alcohol
- Acute Liver Failure
- Poor Nutrition
- Gout
- several Renal Impairment
- Peripheral Neuropathy

PREPERATION OF ANTITUBERCULAR DRUGS[2,3]:

-Isoniazid…….100 -300 mg Tablets

-isoniazid……100mg/5ml Solution

-Isoniazid……...10mg/ml Oral Suspension

-Pyrazinamide …....100mg/ml Oral Solutions

-Cycloserine……..250mg Capsule

-Kenamycin……..0.5-0.75gm/ml Injections

-Rifampicin…….150,300,450mg Capsule

-Rifampicin……300,450,600mg Tablet

TRADE NAMES /BRAND NAMES:

-Isonex

-Isocadipas

-Cadizide

-Rimpazid

-Idipas

MODE OF TRANSMISSION[4]:

- ✓ -It is spread by droplet infection
- ✓ -By direct contact with the patient
- ✓ -By consuming milk derived from a cow suffering from Tuberculosis
- ✓ -By handling sputum and other discharges of the tuberculosis patients
- ✓ -By consuming articles of food and drinks contaminated tubercule bacilli.
- ✓ -When the droplets are expelled by tubercular patient through coughing, sneezing, talking and are inhaled by then healthy person.

SIGNS AND SIMPTOMS OF TUBERCULOSIS:

- Pyrexia (Normally rise in body temperature in evening)
- Fatigue, malaise and loss of body weight.
- Anorexia (Loss of appetite), Night sweat
- Slight palpitation and rapid pulse.
- Chronic cough and hoarseness of throat.
- The breath has peculiar odour and sputum copoious .
- In women suffering from tuberculosis the Mensturation may become absent or scanty.
- Pulmonary artery in tubercle region breaks, which results into massive haemorrhage.

TREATEMENT OF TUBERCULOSIS:

- Drug resistance is the main difficulty in management of tuberculosis hence to avoid it.
- The Antitubercular Agents are always use in combinations.
- The various Therapy advise as follows :

1) PTIMUM ANTITUBERCULAR THERAPY :

In this combination three regiments or Drugs is advised

a) INH +R + S OR E……All Drug given daily for Two Months and followed by;

INH +R……..For Seven Months.

b) INH + R + S + Z…….. Daily for Two Months followed by;

INH + R Twice a Week or Daily Followed by;

INH + S + Z……..Twice a Week for Four Months.

2) **TWO DRUG THERAPY:** This includes Daily a supervise administer of INH + S + E / PAS / T For Two Months Followed by Daily self administration of INH + E/ PAS + T. For 16 Months. In some cases it will be administer up to 22 months.
3) **INTERMITTENT, SUPERVISED TREATMENT:** It includes administration of INH + S or INH + E Twice a Week for 18 Months.
4) **LOW COST REGIME OR DRUGS:** This includes administrations of; INH + R for Two Months Followed by INH + T For 8 Months.

REFERENCES:

1) Goodman & Gilman's, "The Pharmacological Basis of the Therapeutics", 12th Editions 2000, Mcgrwhill publisher, P. 1550-1565.
2) K.D. Tripathi, "Text Book of Essencial of Medical Pharmacology", 6th editions 2008, Jaypee Brothers mrdical publisher, P. 740-750.
3) S.R. Kale & R.R. Kale, "Pharmacology & Toxicology", 13th Edition 2008, Nirali Prakashan, P 171-173.
4) A.K. Gupta, "Handbook of Health Education and Community Pharmacy", 1st Edition reprint 2016, P. 211-215
5) Marcos Abdo Arbex, Marília de Castro Lima Varella, Antituberculosis drugs: Drug interactions, adverse effects, and use in special situations. Part 1: First-line drugs* J Bras Pneumol. 2010; 36(5):626-640.