Anti- Leprotic agents

- Also known as **Hansen's** disease
- It is a chronic granulomatous infection caused by **Mycobacterium leprae**
- Attacks superficial tissues e.g. skin & peripheral nerves
- Organism grow very slowly (org.s can not be cultured in artificial media but grows in foot pad of Armedillon.)

Anti- Leprotic agents

- Disease is still considered as social stigma but it needs a change in the attitude of public to consider it just like any other disease .
- Important is early diagnosis & Tt. which makes it non infectious & prevents compl.s

Anti- Leprotic agents

Anti- Leprotic drugs :

Classification-

-Sulfone- **Dapsone (DDS)**

-Phenazine derivatives- **Clofazimine**

-Antitubercular drugs- **Rifampicin**

Ethionamide

-Other Antibiotics -

Ofloxacin , Minocycline & Clarithromycin

Anti- Leprotic agents

Sulfones -

Derivative of 4-4’ diamino diphenyl sulfone (DDS)

Dapsone:

-Bacteriostatic

-High risk of resistance if used alone

Anti- Leprotic agents

Mechanism:

Similar to sulfonamide i.e. ↓ of dihydrofolate synthase enzyme.(Anti-inflammatory effect occurs via ↓ of tissue damage by neutrophils by ↓ neutrophil myeloperoxidase activity ,↓activity of neutrophil lysosomal enzyme , free radical scavanger ,↓ of migration of neutrophils to the inflammatory sites)

ADRs:

-Nausea , vomiting , anorexia

-Allergic reaction

-Hemolysis in pts with G6PD deficiency

-Methemoglobinaemia

Anti- Leprotic agents

- Neurotoxicity & Psychosis

Sulphone Syndrome:

After 5/6 wks of Tt. in malnourished patients there may be exacerbation of Lepromatous Leprosy similar to Jerisch Hexheimer reaction (seen with Penicillin) ,characterized by fever, malaise , exfoliative dermatitis , lymphadenopathy, Jaundice etc.

Anti- Leprotic agents

Indication –

-Leprosy

-Resistant Malaria (with pyrimethamine)

-Toxoplasma encephalitis in AIDS

-Pneumocystis jirovecii in AIDS

Anti- Leprotic agents

Clofazimine :

It is a dye , weak bactericidal by ↓ the function of DNA.

activity so prevents Lepra reaction.

-used for common skin ulcers & MAC

S/E- Red discolouration of skin

- Eosinophilic enteritis

Anti- Leprotic agents

Rifampicin :

- Important antiTb drug also bactericidal to M. Leprae.
- Rapidly make leprosy Pts noncontagious
- However not satisfactory if used alone- some bacilli persist after prolonged Tt –can cause resistance .

(The congener of Rifampicin - Rifabutin is

Anti- Leprotic agents

also bactericidal against M. leprae but not superior to Rifampicin)

Ethionamide - Has significant antileprotic activity but is hepatotoxic . It can be used as an alternative to Clofazimine but other substitutes are preferred.

Anti- Leprotic agents

Other Antibiotics:

-Fluoroquinolones : **Ofloxacin** , **Pefloxacin**, **Gatifloxacin** are highly active against M. leprae (but not Ciprofloxacin)

-Minocycline: due to high lipophilicity, it is active against M. leprae. , antibacterial activity is less than Rifampicin but more than that of Clarithromycin .

Anti- Leprotic agents

Clarithromycin :

Only macrolide antibiotic having significant activity against M. leprae . It is being included in alternative MDT regimens.

Anti- Leprotic agents

Diagnosis of Leprosy:

Diagnosed with any of the following-

- Skin lesions (hypopigmented patches)
- Impaired or loss of sensation
- Acid fast bacilli in skin smears
- Nerve thickening

Treatment of Leprosy

- India achieved elimination of Leprosy as a public health problem .
- Incidence is less than 1 case/ 10,000 population .

Treatment of Leprosy

Classification:

1. Indeterminate
2. Tuberculoid
3. Borderline
4. Lepromatous
5. Pure neuritis (no skin lesion)

Tuberculoid:

Well defined skin lesion

Treatment of Leprosy

-anesthetic patches

-Organism may or may not be found in skin lesions.

-Lepromine test is positive (diagnostic for Leprosy. It evaluate the immune system of the patient & classify the type of disease.)

-prolonged remission occurs

Treatment of Leprosy

Lepromatous:

-Ill defined skin lesions

-Skin is thickened , glossy & corrugated

-Disease progresses – large nerve trunks get involved – anesthetic patches

-Atrophy of skin & muscles & absorption of small bones e.g. phalanges of extremities, ulceration & spontaneous amputation occurs

Treatment of Leprosy

-Lepromine test is –ve (as cell mediated immunity is absent)

-Smear is +ve for organism .

For treatment purpose –leprosy is classified as-

Multibacillary - It includes lepromatous, borderline cases with +ve skin smear test

Tt- **Rifampicin** - **600 mg / month supervised**

Treatment of Leprosy

Dapsone-100 mg / day self administration

Clofazimine – 300 mg/ month supervised

+ 50 mg/ day self administration

X 2 years- relapse – repeat

Paucibacillary : (small no. of organism)-

It includes indeterminate & tuberculoid

Tt- **Rifampicin** – 600 mg / month supervised

Dapsone – 100 mg / day self administration

X minimum for 6 months-repeat if relapse

Treatment of Leprosy

Single lesion paucibacillary –single dose

ROM- Rifampicin-600 mg + Ofloxacin - 400mg + Minocycline-100 mg

(**MDT was introduced by the WHO in 1981**& was implemented under the **NLEP** (**National Leprosy Eradication Programme**). It includes Dapsone , Rifampicin & Clofazimine . The WHO in 1994 recommended a fixed duration therapy(FDT) of 2 years for MBL & 6 months for PBL . WHO expert committee On Leprosy in 1995 recommended shortening of MDT in MBL to 12 months & this was implemented in our country since 1999 . The purpose of this is to render the Pts noncontiguous & therefore cut down transmission

Treatment of Leprosy

Alternative regimens :

Incorporating newer antileprotic drugs , but these are used only in case of Rifampicin resistance or when MDT is not advisable e.g.-

Clofazimine + any two of Ofloxacin / Minocycline/ Clarithromycin for 6 months followed by Clofazimine + any one of Ofloxacin / Minocycline x additional 18 months .

(**PBL** cases having few bacteria in the body & only one Skin lesion can be treated with single dose of Rifampicin -600 mg + Ofloxacin-400 mg + Minocycline -100 mg. This has been recommended by the **WHO for solitary lesion of PBL**.)

Treatment of Leprosy

Two types of reactional state may occur with therapy

1. **Type I** : Lepra reaction (reversal reaction)
   In borderline leprosy due to increased in host immunity- skin lesion & nerves become swollen & tender without systemic manifestation –
   Tt. –
   Prednisolone (Thalidomide not effective)

Treatment of Leprosy

Type II :Lepra reaction (erythema nodosum leprosum) –observed in lepromatous leprosy – there is skin & nerve manifestation with fever & systemic involvement.

Tt.- by analgesic /antipyretic for mild cases,

in severe cases-**Prednisolone** or **Thalidomide.**

-**Chloroquine** & cytotoxic drugs are also effective.

Treatment of Leprosy

-**Clofazimine** require 3-4 wks so not suitable for acute cases, **but useful in chronic cases & prevention of this reaction** .

- **No need to stop the anti- leprotic drugs** .

WHO Recommended Regimen

- **Tuberculoid** - Dapsone 100mg/d and rifampicin 600mg (6 months)

- Lepromatus - dapsone 100mg/d , Clofaximine 50mg/d and

  Rimfampicin 600mg (12 months)

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