Anti-Leprotic Drugs

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Coating

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Cheomothery

Anti-Leprotic

- ✓ Leprosy is caused by Mycobacterium laprae, a rod shaped bacillus that is an obligate intracellular (only grows inside of certain human and animal cells) bacterium.

Transmission

- ✓ Droplets and other secretion can contain the bacteria that causes Hansen's disease.
- ✓ Disease can spread from person to person when some one with the disease cough or sneezes. This cam release droplets into the air.

Leprosy

Symptoms

- ✓ Primarily affected the skin, nerves out side the brain and spinal cord.
- ✓ Disfiguring skin sores, lumps or bumps.
- ✓ Skin sores are pale-colored
- ✓ Loss of feeling in the arm and legs

- Obligate intracellular bacilli.
- Acid-fast
- Reductive evolution
- Cell wall contains PGL-1, Triglycerides
- Grows in cooler tissue.
- Doubling time 14 days.

Leprosy

Types of leprosy

Tuberculoide (Paucibacillary)

- ✓ Mild, less severe form of leprosy.
- ✓ People with this type have only one or few patches of flat, pale colored skin.
- ✓ The affected area of skin may feel numbs because of nerve damage underneath.
- ✓ Tuberculoide leprosy is less contagious than other.

Leprosy

Lepromatous (Multibacillary)

- ✓ A more severe form of the disease. It has wide spread skin bumps, rashes (Multibacillary leprosy), numbness and weakness.
- ✓ The nose, kidneys and male reproductive organs may also be affected.
- ✓ It has more contagious than Tuberculoide leprosy form.

Leprosy

Classification

1. **Sulfone**
   e.g. Dapsone (DDS)
2. **Phenazine derivative**
   e.g. Clofazimine
3. **Anti-tubercular drugs**
   e.g. Rifampin, Ethionamide
4. **Other antibiotics**
   e.g. Ofloxacin, Moxifloxacin, Minocycline, Clarithromycin

Leprosy

Diagnostic test

- ✓ Skin leprosy: Doctors remove a small sample of abdominal skin and send it to a lab to be examinees.
- ✓ Skin smear test

Result of test

- ✓ In Paucibacillary leprosy, no bacteria will be detected, in contrast, bacteria are expected to be found on a skin smear test form a person with Multibacillary leprosy.

Leprosy

Dapsone (DDS)

Diaminodiphenyl sulfone

- ✓ Dapsone is most widely used sulfone for the long term therapy.
- ✓ Although the sulfones are highly effective against most strains of M. laprae.

MOA

- ✓ The sulfones are structural analogues of PABA and are competitive inhibitor of **folic acid synthesis**.
- ✓ Sulfones are bacteriostatic and are used only in the treatment of leprosy.
- ✓ **Combination:** Rifampicin and Clofazimine.

Pharmacokinetics

- ✓ Well absorbed orally and widely distributed throughout body fluid and tissue.
- ✓ Peak concentration is 1-3 hours.
- ✓ Oral half life 21-44 hours.
- ✓ 50% bound to serum proteins.
- ✓ Sulfone tends to remain skin, muscle, kidney and liver up to 3 weeks after therapy is stopped.
- ✓ The concentration in inflamed skin is 10 to 15 times higher than that found in the normal skin.
- ✓ Retained for long term (12-35 days) because of hepatobiliary drug circulation.
- ✓ Metabolized by liver (Acetylation)
- ✓ 70-80% drug is excreted in the urine as metabolites.

Leprosy

Uses

- ✓ Dapsone combined with other anti-leprotic agents like rifampin and Clofazimine.
- ✓ Used in the treatment of both Multibacillary and paucibacillary M. Laprae infections.

Adverse effects

- ✓ Mild haemolytic anaemia.
- ✓ Gastric intolerance
- ✓ Cutaneous reaction: Allergic rashes, hypermelanosis, photo toxicity and rarely exfoliative dermatitis.
- ✓ Hepatitis and agranulocytes are rare complication.
- ✓ Sulfone syndromes: develops 4-6 weeks after starting Dapsone treatment: consist of fever malaise, lymph node enlargement, jaundice and anaemia.
- ✓ Treatment: stopping Dapsone and starting corticosteroid therapy along with supportive measures.

Leprosy

Contraindication

- ✓ Should not used in severe anaemia (Hb <7g/dl).
- ✓ Hypersensitivity reaction.
- ✓ glucose-6-phosphate dehydrogenase deficiency.

Leprosy

Clofazimine

- ✓ It has leprostatic and anti-inflammatory properties.

MOA

- ✓ Interference with template fusion of DNA in M. leprae.
- ✓ alteration of membrane structure and its transport function.
- ✓ Disruption of mitochondrial electron transport chain.

ADME

- ✓ Orally active (40-70% absorbed)
- ✓ It accumulated in macrophages and gets deposited in many tissues including subcutaneous fat, as needle shaped crystals.
- ✓ Entry in CSF is poor.
- ✓ t ½ is 70 days so that intermittent therapy is possible.

Leprosy

Uses

- ✓ Clofazimine shows anti-inflammatory property, so it is valuable in leprae reaction.

Adverse effects

- ✓ **Skin:** Radish black discoloration of skin.
- ✓ Discoloration of hair and body secretion.
- ✓ Dryness of skin and itching.
- ✓ Acneiform eruptions
- ✓ Phototoxicity
- ✓ **GI symptoms:** Nausea, vomiting, abdominal pain, weight loss and intermittent loose stool.
- ✓ **Late syndrome:** deposition of Clofazimine crystal in the intestinal submucosa.

Rifampin (R)

- ✓ Most potent cidal drug for M. leprae.
- ✓ More effective: given once a month.
- ✓ Given to patients with hepatic or renal dysfunction as well as during **Erythema nodosum leprosum (ENL)** and reversal reaction in leprosy patients, because it can release large quantity of Mycobacterial antigen by inducing rapid bacillary killing.

Leprosy

Ofloxacin

- ✓ Cidal M. leprae
- ✓ Can be used alternative regiments in case rifampicin cannot be used.
- ✓ To shorten the duration of treatment.
- ✓ Reduce chances of drug resistance.

Drugs	Multibacillary	Paucibacillary
Rifampin	600mg once a month	600mg once a month supervised
Dapsone	100mg daily self administration	100mg daily self administered
Clofazimine	300mg once a month supervised and 50mg daily self administered.	--
Duration	12 months	6 months

Leprosy

Alternative regimens

- ✓ Intermittent (ROM)
  - ✓ Rifampin 600mg
  - ✓ Ofloxacin 400mg
  - ✓ Minocycline 100mg

  Once a month for 3-6 month (PBL) & 12-24 months for (MBL)

- ✓ Intermittent (RMM)
  - ✓ Rifampin 600mg
  - ✓ Moxifloxacin 400mg
  - ✓ Minocycline 200mg

  Once a month 6 doses given PBL and 12 doses given for MBL cases

Lepra reaction

- ✓ Temporary discontinuation of Dapsone is recommended only in severe cases.
- ✓ Clofazimine (200mg daily) is effective in controlling the reaction (except the severe one).
- ✓ Prednisolone 40-60mg/day for severe reaction.

Multidrug therapy (MDT)

- In case the dapsone resistant strain, multidrug therapy with **rifampin, clofazimine** was introduced by the WHO in **1981**.
- And was implemented by **NLEP** (National Leprosy Eradication Programme) in **1982**.

Advantages of MDT

- Effective in cases with primary dapsone resistance.
- Prevents emergence of dapsone resistance.
- Reduce total duration of therapy.

Leprosy

MDT of Leprosy

Drugs	MBL	PBL
Rifampin	600mg once a month supervised	600mg once a month supervised
Dapsone	100mg daily self administered	100mg daily self administered
Clofazimine	300 mg once a month supervised and 50 mg daily self administered	—
Duration	12 months	6 months
Dose to be reduced suitable for children		

Leprosy

Leprosy

Thank you