

ANTILEPROTIC DRUGS:

leprosy caused *H. leproe* - chronic infections.

ANTILEPROTIC DRUGS

sulfone
→ Dapsone

phenazine derivative
- clofazimine

Anti-TB drugs
Rifampin
Ethionamide

Other Antibiotics
- Ofloxacin
- Moxifloxacin
- Minocycline
- Clarithromycin

DAPSONE (DDS) - Diamino diphenyl sulfone. ^{Inhibit}

MOA: Chemically Related to sulfonamides i.e., PABA incorporation into folic Acid by folate synthase.

- *lepra bacilli* utilize PABA for the synthesis of folic Acid which is needed for the growth & development (multiplication)

- Dapsone is structurally similar to PABA hence competitively inhibits folate synthase enzyme & prevent the formation of THFA.
Thus leprostatic effect.

Para-Amino benzoic Acid

DAPSONE $\xrightarrow{E}$

FOLATE SYNTHASE

Dihydrofolic Acid

→ This needed for the bae growth.

↓

Dihydrofolic Reductase

THFA
(Tetrahydrofolic Acid)

⇒ specificity is due to the affinity of its folate synthase enzyme.

PK: orally, Absorbed from gut.
bound to plasma protein.
Metabolized by Acetylation of Metabolites.

ADR: dose Related hemolytic Anemia in G6PD deficiency

Gastric intolerance: nausea, vomiting, fever, headache, dermatitis,
Methemoglobinemia.

CI → In Anemia, G6PD, hypersensitivity.

Sulfone syndrome: This Rⁿ develops 4-6 weeks after daprone + f.
consist of fever, malaise, lymph node enlargement, desquamation of skin,
jaundice of Anemia (seen in malnourished person).

more frequent with MDR. ~~may also occur~~ stoppage of daprone

other use → use for chloroquine Resistant Malaria, P. falciparum infection.

(LOFAZIKINE (Clz):

It is a phenazine dye & has leprostatic Activity against leprobacteria
has Anti-inflammatory effect so useful in Type 2 Leprosy Reaction.

MOA: This bind with mycobacterium DNA to inhibit its template function.

↓
Alteration of membrane structure of its transport function

↓
Disruption of mitochondrial electron transport chain.

→ used in daprone Resistant organism.

PK → orally Active.

It accumulate in macrophages as needle shaped crystals in many tissue
including Absorption subcutaneous fat.

→ used in MDR

ADR → Reddish, Black discoloration of skin, hair, body secretion.
Aches from eruption & phototoxicity.

GI → Nausea, vomiting, Abdominal pain, weight loss

Clf → pregnancy, liver disease.

TREATMENT OF LEPROSY: - 1 year + / 2 years

For HBL (LL, BL, BB)

→ Rifampin 600mg once monthly +

→ Dapsone 100mg

→ Clofazimine 30mg

For PBL (PP, BT, P) → Dapsone, Rifampin for 6 months

Alternative Regimens → Clofazimine + Any two newer drugs (Moxifloxacin, Ofloxacin)

REACTION IN LEPROSY:

Type II These are immunologically mediated Rⁿ that occur during the course of the disease. mild, severe or life threatening Rⁿ is erythema nodosum leprosum (ENL) ^{occurs in LL}
lepra Rⁿ is of abrupt onset, existing lesion enlarge, become red, swollen
Malaise, fever may appear

⇒ Clofazimine is effective in controlling the Rⁿ

⇒ For severe Rⁿ - Prednisolone - 40-60mg/day

THALIDOMIDE: It can be used in ENL

It is Anti-inflammatory, cytokine modulating drug.

→ Type III hypersensitivity due to Release of Antigen from the dying of leprobacteria

~~Re~~ REVERSAL REACTION: delayed type of hypersensitivity seen in TT, BT

cutaneous ulceration, multiple nerve involvement with swollen, painful, tender
nerve occur suddenly after completion of therapy

tft with clofazimine or corticosteroids.

Thalidomide ineffective.