CO-TRIMOXAZOLE

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COTRIMOXAZOLE

- (TRIMethoprim + SulfamethOXAZOLE)

Rationale :-

- WHO - approved Fixed Dose Combination (FDC)
- The ratio of Sulfamethoxazole : Trimethoprim is 5:1, which is fixed in order to achieve peak optimal plasma concentration of 20:1. Produces synergistic effect in blood & tissues.
- Closely Matchable Half – life

Cotrimoxazole (Rationale…contd)

- Bactericidal (Given alone is Bacteriostatic)
- Wider spectrum (Both Gm +ve, Gm –Ve)
- Development of resistance is delayed
- Trimethoprim → good conc. in CSF
- High degree of selective affinity for bacterial DHFR enzyme by Trimethoprim

ANTIBACTERIAL SPECTRUM

- Gram +ve & Gm –Ve organisms (Staph. Aureus, streptococci,meningococci, C. diptheriae, E. Coli, Proteus, H. influenzae, Salmonella & shigella).
- Chlamydiae -→ useful in Chlam. Trachomatis
- Pneumococci
- Pneumocystis jiroveci (Carinii) -→ secondary infections occuring in immunocompromised AIDS patient. (Other drugs used in Pn. Jiroveci are :- Pentamidine, Clindamycin, Primaquine, Atovaquone).

Mechanism of Action of Cotrimoxazole

PABA

↓

Folic acid synthetase ↓ ***Sulphamethoxazole***

Dihydrofolic acid (DHF)

Dihydrofolate reductase ↓ ***Trimethoprim***

Tetrahydrofolic acid (THF)

↓

Folic acid synthesis inhibited

Mechanism of Action (contd…)

- Cotrimoxazole produces sequential blockade to inhibit bacterial folic acid synthesis
- Two drugs interfere with two successive steps in the same metabolic pathway & produce supra-additive effect
- Sulfamethoxazole inhibits folate synthetase whereas Trimethoprim inhibits folate reductase enzyme.

RESISTANCE : slowly developed

- produce increased amounts of PABA
- adopt an alternative pathway in folate metabolism.
- Alteration in dihydropteroic acid synthetase

PHARMACOKINETICS

- Orally well absorbed. Also given parenterally
- Plasma protein binding good
- Achieve higher conc. in tissues & body fluids like prostate, vagina, CSF and sputum
- Metabolized by acetylation in liver & excreted in urine.

ADVERSE EFFECTS

- Skin & GIT disturbances
- Stevens – Johnson syndrome (Fever, erythema multiforme,exfoliative dermatitis & mucous membrane ulceration)
- Megaloblastic anaemia due to folate deficiency in alcoholics & malnourished persons. N,V, stomatitis & glossitis.
- Bone marrow suppression with leukopenia, neutropenia & thrombocytopenia in elderly
- C/I in pregnancy

USES of Co-trimoxazole

1. Acute urinary tract infections due to Gm – ve organism like E.coli, proteus & Enterobacter spp. (Cotrimoxazole - DS Tabs foe 3 days.

2. Chronic & Recurrent UTIs in women

3. Prostatitis in male

4. Acute & chronic respiratory tract infections due to S. pnuemoniae & H. influenzae.

   Acute sinusitis, bronchitis, otitis media

5. Typhoid (Enteric fever) → resistance developed

6. Bacterial diarrhoeas & dysentry due to E.coli, Shigella & salmonella spp.

7. Sexually Transmitted Diseases (STDs)- Chanchroid due to H. Ducreyi.

8. Pneumocystitis jiroveci (carinni) in AIDS pts

IV COTRIMOXAZOLE :-

- In 5% dextrose
- pneumocystitis jeroveci
  typhoid fever
  gram –ve bactermia

- **TABS :-**
- **Sulfamethoxazole 400mg + Trimethoprim 80 mg**
- **Sulfamethoxazole 800mg + Trimethoprim 160 mg (Cotrimoxazole – DS Tabs)**

CLINICAL ASPECTS

- **Cotrimoxazole is inexpensive & hence widely used**
- **Currently cotrimoxazole use is restricted to the treatment of Pneumocystis jiroveci & toxoplasmosis**
- **First line drug in UTIs before culture –till report available**
- **Allergic reactions to be considered before using it.**

THANK YOU