AMPICILLIN

CLASS.

Ampicillin - a semisynthetic extended spectrum penicillin antibiotic

PHARMACOLOGY.

Mechanism of action :

Ampicillin like all penicillins interferes with last step in bacterial cell wall synthesis. Penicillin binds with Penicillin binding proteins (PBP) and inhibits carboxypeptidases, endopeptidases and transpeptidases necessary for cross linking of peptydoglycon chains which gives rigidity to the bacterial cell wall. Penicillin are effective against multiplying organisms and are bactericidal.

Effect on organ systems :

Spectrum of activity -

- Gram+ve and some gram -ve bacteria.
- Some aerobic gram-ve.
- Some spirochetes.

Resistance -

- β-lactamase - hydrolyses the cyclic amide bond of β-lactum ring which results in loss of activity.
- Decreased penetration through outer cell membrane prevents drug from reaching P.B.P.
- Alteration in P.B.P. binding sites.

Adverse Reactions -

- Hypersensitivity - Common with all penicillin - Incidence nearly 10%. Major cause is penicillin metabolite penicilloic acid, which reacts with proteins and serves as heptane to cause immune reaction. Reaction may range from urticaria to angioedema (swelling of lips, tongue and periorbital area) and anaphylaxis.
- Ampicillin rash - produces erythematous, maculopapular rash over most of trunk. Rash is mild and subside in 7-14 days even though ampicillin is continued.
- Superinfection - with pseudomonas, staphylococci, proteus or candida albicans.

CHLORAMPHENICOL

CLASS.

Chloramphenicol - borad spectrum antibiotic

PHARMACOLOGY.

Mechanism of action :

Chloramphenicol inhibits microbial protein synthesis by binding reversibly to a receptor site on 30- S subunit of bacterial ribosome. This site of action is also shared by erythromycin and clindamycin. There it interferes with the incorporation of amino acids into newly formed peptides by blocking the action of peptidyl transferase. Chloramphenicol is bacteriostatic

Effect on organ systems

GIT - Nausea, vomiting, diarrhoea. Alteration in microbial flora may cause candidiasis of mucous membrane (mouth and vagina)

Bone Marrow- Disturbance of RBC maturation after 1-2 week of drug administration. Vacuolated nucleated red cells in marrow, anemia and reticulocytopenia with rise in serum iron concentration and depression in serum phenylalanine levels.

Blood - Aplastic anemia - commonly a genetically determined idiosyncratic reaction, unrelated to dose but common with prolong duration of chloramphenical administration. It may be irreversible and fatal. Aplastic anemia may occur after therapy has ceased.

New Born - Grey Baby Syndrome - Neonates have low capacity to glucuronidate chloramphenicol which is essential for its degradation and detoxification. Coupled with under developed kidneys in the neonate, the drug accumulate. The syndrome is characterized by vomiting flaccidity, hypothermia, grey colour of skin, shock and collapse.

PHARMACOKINETICS

- Chloramphenicol is lipophilic in nature and is completely absorbed on oral administration. The drug is inactivated in liver by conjugation with glucuronic acid or by reduction to inactive arylamine. The inactivated products (90%) are secreted by renal tubules. Only 10% of active drug is excreted by glomerular filtration. Chloramphenicol is widely distributed in body including brain tissue where its concentration may be equal to that in serum.

COTRIMOXAZOLE

CLASS.

Cotrimoxazole - is a combination of antifolate and an anti-infective agent.

PHARMACOLOGY.

Mechanism of action :

Cotrimoxazole is a combination of trimethoprim and sulfamethoxazole.

- ➤ The synergistic antimicrobial activity results from two sequential steps in the synthesis of tetrahydrofolic acid.
- ➤ Sulfamethoxazole (SMX) competes with PABA for incorporation with the pathway and then inhibits dihydropteroate synthetase.
- ➤ Trimethoprim (TMP) inhibits dihydrofolate reductase the enzyme responsible for converting dihydrofolic acid to tetrahydrofolic acid.
- ➤ The lack of folic acid inhibits thymidine synthesis.

Spectrum -

The combination is usually bactericidal although separately. SMX is bacteriostatic while TMP is bactericidal. The combination has broader spectrum than the sulfas. Most gram+ve and gram-ve (esp. Shigella) bacteria. No anaerobic spectrum. Pneumocystis carinii (protozoa) infection.

Resistance -

usually plasmid mediated - develop more slowly for combination than either drug alone.

Resistance may result from :

a) alteration in production or sensitivity of DHFR.
b) decreased permeability of cotrimoxazole into bacteria.
c) increase in synthesis of enzyme (upto 70 times).
d) bacteria utilizes preformed folic acid instead.

Effect on organ system :

Hypersensitivity -These are more common and may be severe in elderly. These include exfoliative dermatitis. Stevens-Johnson syndrome, serum sickness and allergic myocarditis. Other manifestations include anaphylaxis, arthralgia and various rashes.

Eyes Photophobia, diplopia, abnormal color perception.

PHARMACOKINETICS :

Not metabolized and eliminated principally by kidneys unchanged. Half life is about 36 hours. but is significantly prolonged by impaired renal function.

THERAPEUTIC USES.

- Low out-put cardiac failure.
- Atrial fibrillation and flutter
- Paroxysmal atrial tacycardia.

CONTRAINDICATIONS

- Cardiac tamponade, high out-put CHF, constrictive pericarditis and ideopathic hypertrophic subaortic stensois with output obstruction.

ION CONCENTRATION

Potassium - Digoxin competes with K^+ for binding sites on the sodium pump. Generally↑ extracellular K^+ inhibits binding and reduce efficacy, while K^+ enhances activity leadiing to toxicity.

Calcium - Acts synergistically. Low Ca^{++} leads to ↓ effect of digoxin. Concomitant administration enhances ectopic stimuli formation and can lead to ventricular tacharrhythmias.