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MECHANISM OF ACTION OF MACROLIDES AND ERYTHROMYCIN, DISEASES IN WHICH ERYTHROMYCIN IS USED

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Annotation

Macrolides are antibiotics with a large (macrocyclic) lactone ring to which sugars are attached. Erythromycin and its semisynthetic derivatives roxithromycin, clarithromycin and azithromycin are the macrolides currently used. Dirithromycin, oleandomycin, troleandomycin and spiramycin are other macrolide antibiotics. Erythromycin is obtained from Streptomyces erythreus.

Key words: Erythromycin has a narrow spectrum and is effective against aerobic gram-positive bacteria and a few gram-negative organisms. Streptococci, pneumococci, staphylococci, gonococci, legionella, C. diphtheriae, B. pertussis, T. pallidum, C. jejuni, Mycoplasma, Chlamydiae and some atypical mycobacteria are sensitive.

Erythromycin is bacteriostatic at low and cidal at high concentrations. It is more effective in the alkaline pH. It binds to 50S ribosomes and inhibits bacterial protein synthesis. Macrolides inhibit the translocation of the growing peptide chain from A site to P site. Hence, A site is not available for binding of the next amino acid (brought by t-RNA) and protein synthesis stops. Chloramphenicol and clindamycin also bind to 50S ribosomes and the three may antagonise each others activity because they compete for the same binding site. Hence, the combination should be avoided.

Resistance to macrolides is acquired through plasmids. The mechanism of expression of resistance may be:

Low permeability of the bacteria to the antibiotic.

Production of inactivating enzymes that hydrolyze macrolides.

Low affinity of ribosomes to macrolides— such organisms are also resistant to other drugs which bind 50s ribosomes—lincosamides and streptogramins called macrolide-lincosamide-streptogramin or MLS-type resistance.

Pharmacokinetics. Food interferes with absorption. Among the different salts, erythromycin estolate is the best absorbed, but not preferred due to risk of adverse effects. Erythromycin is destroyed by gastric acid and is, therefore, given as enteric coated tablets. Plasma t½ ~1.5 hr. Good concentration is attained in most fluids except brain and CSF. It also crosses the placenta. Erythromycin is a microsomal enzyme inhibitor. It is mainly excreted through the bile; dose adjustment is not needed in renal failure.

Adverse Effects: hepatitis with cholestatic jaundice starts after 2–3 weeks of treatment and incidence is more common with the estolate salt. The symptoms—nausea, vomiting and abdominal cramps, mimic acute cholecystitis and may be wrongly treated. These are followed by jaundice and fever. It may be an allergic response to the estolate salt. Hepatitis is self-limiting but erythromycin should be avoided in such patients as they are likely to develop hepatitis again.

Epigastric distress, nausea, vomiting and diarrhoea are often reported. Erythromycin is a motilin receptor agonist due to which it causes increased intestinal motility.

Allergic reactions including fever and skin rashes can occur.

Cardiac arrhythmias are reported in patients with cardiac diseases or on other arrhythmogenic drugs.

Erythromycin can also cause reversible hearing impairment in some patients.

Drug Interactions. Erythromycin and clarithromycin are microsomal enzyme (cytochrome P450) inhibitors. They inhibit the hepatic metabolism and thereby enhance the plasma levels of other drugs like carbamazepine, terfenadine, theophylline, valproate, digoxin and warfarin resulting in toxicity due to these drugs. Erythromycin can be used as an alternative to penicillin in patients allergic to penicillin.

Atypical pneumonia: May be caused by agents like Mycoplasma, Chlamydia and Legionella. Atypical pneumonia due to Mycoplasma pneumoniae—erythromycin is the drug of choice - 500 mg 6 hourly oral.

Legionnaires' pneumonia: It is treated for 10–14 days with erythromycin. Azithromycin is now considered the drug of choice.

Whooping cough: Erythromycin is the drug of choice for the treatment and postexposure prophylaxis of close contacts. Clarithromycin and azithromycin may also be used.

Streptococcal infections: Pharyngitis, tonsillitis and scarlet fever respond to erythromycin. Staphylococcal infections: minor infections may be treated but now resistant strains are common. Diphtheria: Erythromycin is very effective in acute stage though antitoxin is life saving. Erythromycin also eradicates the carrier state. Other uses: a. Erythromycin is a motilin receptor agonist and stimulates GI motility. This property can be made use of in gastroparesis in postoperative patients and in diabetic gastroparesis. b. Erythromycin has been found to have anti-inflammatory actions and may be of value in rheumatoid arthritis and chronic sinusitis.

All in all, antibiotics such as erythromycin will not work for colds, flu, or other viral infections. Taking antibiotics when they are not needed increases your risk of getting an infection later that resists antibiotic treatment. Erythromycin is in a class of medications called macrolide antibiotics. It also is used to prevent recurrent rheumatic fever. It works by stopping the growth of bacteria.

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