Name: Fashoro Mary Olakorede
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MACROLIDES

The macrolides are a class of natural products that consist of a large macrocyclic lactone ring to which one or more deoxy sugars, usually cladinose and desosamine, may be attached. The lactone rings are usually 14-, 15-, or 16-membered. Macrolides belong to the polyketide class of natural products.
Examples of macrolides include Azithromycin, Clarithromycin, Erythromycin and Fidaxomicin

THE MECHANISM OF ACTION

Macrolides are inhibitors of bacterial protein biosynthesis, and they do this by preventing peptidyltransferase from adding the growing peptide attached to tRNA to the next amino acid (similar to chloramphenicol) as well as inhibiting ribosomal translation on the 50s ribosomal subunit. Another mechanism is premature dissociation of the peptidyl-tRNA from the ribosome.
Macrolide antibiotics do so by binding reversibly to the P site on the 50S subunit of the bacterial ribosome. This action is considered to be bacteriostatic. Macrolides are actively concentrated within leukocytes, and thus are transported into the site of infection.

INDICATION FOR USE

The antimicrobial spectrum of macrolides is slightly wider than that of penicillin, and, therefore, macrolides are a common substitute for patients with a penicillin allergy. Beta-hemolytic streptococci, pneumococci, staphylococci, and enterococci are usually susceptible to macrolides. Unlike penicillin, macrolides have been shown to be effective against Legionella pneumophila, mycoplasma, mycobacteria, some rickettsia, and chlamydia. Macrolides are also used to treat infections caused by Gram-positive bacteria (e.g., Streptococcus pneumoniae) and limited Gram-negative bacteria(e.g., Bordetella pertussis, Haemophilus influenzae), and some respiratory tract and soft-tissue infections.

TOXICITY

Macrolides should not be taken with colchicine as it may lead to colchicine toxicity. Symptoms of colchicine toxicity include gastrointestinal upset, fever, myalgia, pancytopenia, and organ failure.

ADVERSE EFFECTS

The combination of some macrolides and statins(used for lowering cholesterol) is not advisable and can lead to debilitating myopathy. This is because some macrolides (clarithromycin and erythromycin, not azithromycin) are potent inhibitors of the cytochrome P450 system, particularly of CYP3A4. Macrolides, mainly erythromycin and clarithromycin, also have a class effect of QT prolongation, which can lead to torsades de pointes. Macrolides exhibit enterohepatic recycling; that is, the drug is absorbed in the gut and sent to the liver, only to be excreted into the duodenum in bile from the liver. This can lead to a buildup of the product in the

system, thereby causing nausea. In infants the use of erythromycin has been associated with pyloric stenosis.

Some macrolides are also known to cause cholestasis, a condition where bile cannot flow from the liver to the duodenum. A new study found an association between erythromycin use during infancy and developing IHPS (Infantile hypertrophic pyloric stenosis) in infants. However, no significant association was found between macrolides use during pregnancy or breastfeeding.