Adverse effects

included constipation, nausea, headache, myalgias and insomnia. Increased hepatic transaminases and also elevations in creatine phosphokinases occurred, suggesting weekly monitoring of these enzymes, while the patient is receiving daptomycin. Statins should be discontinued while receiving daptomycin due to the potential for additive muscle toxicity.

TELAVANCIN

Telavancin is a semi-synthetic lipoglycopeptide antibiotic that is a synthetic derivative of vancomycin. It is an alternative to vancomycin, daptomycin, linezolid, and quinupristin/dalfopristin in treating complicated skin and skin structure infections caused by resistant gram-positive organisms, including MRSA.

Mechanism of action

Like vancomycin, telavancin inhibits bacterial cell wall synthesis. Unlike vancomycin, telavancin exhibits an additional mechanism of action similar to that of daptomycin, that involves disruption of the bacterial cell membrane.

Antibacterial spectrum

Telavancin is bactericidal against methicillin-resistant Staphylococcus aureus (MRSA), Streptococcus pyogenes, Streptococcus agalactiae, penicillin-resistant Streptococcus pneumoniae, Streptococcus angiosus group, and vancomycin-susceptible Enterococcuss faecalis isolates.

Telavancin is an alternative to vancomycin, Telavancin is not effective versus E. faecium or VRE.

Pharmacokinetics

Telavancin undergoes hepatic metabolism, it has a half-life of 7 to 9 hours. It is given by IV infusion and renal function should be monitored during therapy, and dose is adjusted according to renal function.

Adverse Effects

The most common adverse reactions reported with telavancin have included taste disturbances, nausea, vomiting, insomnia, and foamy urine. Telavancin is not recommended during pregnancy.

Because telavancin may prolong the QTc interval, use should be avoided in patients with a history of QTc prolongation, uncompensated heart failure, severe left ventricular hypertrophy, or patients receiving other medications that may prolong the QTc interval. Telavancin may also interfere with tests used to monitor coagulation (e.g , Prothrombine time, INR).

Pharmacokinetics

Slow IV infusion (60–90 minutes) of vancomycin is employed for treatment of systemic infections or for prophylaxis. Because vancomycin is not absorbed after oral dministration, this route is employed only for the treatment of antibiotic-induced colitis due to C. difficile.

Metabolism of the drug is minimal, and 90 to 100 percent is excreted by glomerular filtration

Dosage must be adjusted in renal dysfunction, because the drug will accumulate.

Adverse effects

Side effects are a serious problem with vancomycin and include fever, chills, and/or phlebitis at the infusion site. Flushing ("red man syndrome") and shock result from histamine release associated with a rapid infusion.

Also dose-related hearing loss has occurred in patients with renal failure who accumulate the drug. Ototoxicity and nephrotoxicity are more common when vancomycin is administered with another drug (for example, an aminoglycoside) having similar toxicity.

G+ → DAPTOMYCIN

Daptomycin

Daptomycin is a cyclic lipopeptide antibiotic that is an alternative to other agents, such as linezolid and quinupristin/dalfopristin, for treating infections caused by resistant gram-positive organisms, including MRSA and vancomycin-resistant enterococci (VRE).

mechanism

Upon binding to the bacterial cytoplasmic membrane, daptomycin induces rapid depolarization of the membrane, thus disrupting multiple aspects of membrane function and inhibiting intracellular synthesis of DNA, RNA, and protein. Daptomycin is bactericidal.

Antibacterial spectrum

Daptomycin has a spectrum of activity limited to gram-positive organisms, which includes MSSA, MRSA, penicillin-resistant Streptococcus pneumoniae, Streptococcus pyogenes, Corynebacterium jeikeium, E. faecalis, and E. faecium (including VRE). Daptomycin is indicated for the treatment of complicated skin and skin structure infections and bacteremia caused by S. aureus.

daptomycin is inactivated by pulmonary surfactants; thus, it should never be used in the treatment of pneumonia.

Pharmacokinetics

Daptomycin is 90 to 95 percent protein bound and does not appear to undergo hepatic metabolism; however, the dosing interval needs to be extended from every 24 hours to every 48 hours in patients with severe renal impairment.

- G+ + VRE
- skin + bacteremia by S. aureus

β-LACTAMASE INHIBITORS

β-Lactamase inhibitors, such as clavulanic acid, sulbactam, and tazobactam contain a β-lactam ring, but by themselves, do not have significant antibacterial activity. Instead, they bind to and inactivate β-lactamases, thereby protecting the antibiotics that are normally substrates for these enzymes. The β-lactamase inhibitors are therefore formulated in combination with β-lactamase sensitive antibiotics.

VANCOMYCIN

Vancomycin has become important because of its effectiveness against multiple drug-resistant organisms, such as MRSA and enterococci. However, emergence of vancomycin resistance in these organisms. Two examples are vancomycin resistant enterococci (VRE) and increased MICs of MRSA.

Mechanism of action

Vancomycin inhibits synthesis of bacterial cell wall phospholipids as well as peptidoglycan polymerization by binding to the D-Ala-D-Ala side chain of the precursor pentapeptide.

This prevents the transglycosylation step in peptidoglycan polymerization, thus weakening the cell wall and damaging the underlying cell membrane.

Antibacterial spectrum

* Vancomycin is effective against gram-positive organisms. It has been lifesaving in the treatment of MRSA and methicillin-resistant Staphylococcus epidermidis (MRSE) infections as well as enterococcal infections.
* To prevent emergence of resistance (for example, resistant Enterococcus faecium and Enterococcus faecalis), vancomycin should be used only in the treatment of serious infections caused by β-lactam resistant, gram-positive microorganisms or for patients with gram-positive infections who have a serious allergy to the β-lactams.
* Oral vancomycin is limited to treatment for potentially life-threatening, antibiotic-associated colitis due to C. difficile. Intravenous vancomycin is used in individuals with prosthetic heart valves and in patients undergoing implantation with prosthetic devices, especially when there is a risk of MRSA or MRSE.
* Vancomycin acts synergistically with the aminoglycosides, and this combination can be used in the treatment of enterococcal endocarditis.

Resistance

Vancomycin resistance can be caused by plasmid-mediated changes in permeability to the drug or by decreased binding of vancomycin to receptor molecules.

- inhibitor of cell wall synthesis + Peptidoglycan Polymerization
- slow I.V 60-90 min
(X transglycosylation)