

Polymyxin B*

Class: Polymyxins

Overview

Polymyxin B is a polypeptide bactericidal antibiotic. The polymyxins were discovered in 1947 and introduced to the medical community in the 1950s. Colistin, also called polymyxin E and its parenteral form, colistimethate, are related polymyxins. Polymyxins can be administered orally, topically or parenterally, including intrathecally and intraperitoneally. However parenteral administration is primarily used in life threatening infections caused by Gram-negative bacilli or *Pseudomonas* species that are resistant to other drugs. Polymyxins exert their effect on the bacterial cell membrane by affecting phospholipids and interfering with membrane function and permeability, which results in cell death. Polymyxins are more effective against Gram-negative than Gram-positive bacteria and are effective against all Gram-negative bacteria except *Proteus* species. These antibiotics act synergistically with potentiated sulfonamides, tetracyclines and certain other antimicrobials. Polymyxins also limit activity of endotoxins in body fluids and therefore, may be beneficial in therapy for endotoxemia.

Polymyxins are not well absorbed into the blood after either oral or topical administration. Polymyxins bind to cell membranes, purulent exudates and tissue debris. The drugs are eliminated from the kidneys with approximately sixty percent of polymyxin B and ninety percent of colistin excreted unchanged. Polymyxins are considered nephrotoxic and neurotoxic and neuromuscular blockade is seen at higher concentrations. In reality, the potential for nephrotoxicity is minimal when the drugs are utilized properly, especially colistin. Polymyxin B is a potent releaser of histamines and hypersensitivity reactions can occur. Parenteral polymyxins are often characterized by intense pain at the injection site. Divalent cations, unsaturated fatty acids and quaternary ammonium compounds inhibit the activity of polymyxins.

Resistance

Resistance to polymyxins is uncommon and is exclusively chromosome dependent. The paucity of development of resistance is likely due to the drugs' unique detergent action on the cell membrane. However, development of resistance to colistin in *Pseudomonas aeruginosa* is not uncommon with long term inhalation therapy for cystic fibrosis.

Effectiveness

Polymyxin B is commonly applied topically for otitis externa and other surface infections. The relatively narrow antibacterial spectrum often includes *Acinetobacter*, *Enterobacter*, *Klebsiella*, *Salmonella*, *Pasteurella*, *Bordetella* and *Shigella* species and *E. coli*. The drug is not effective against most *Proteus* species.

In human medicine there is renewed interest in use of colistin and polymyxin B as therapy for urinary tract infections, ventilator-associated pneumonias, cystic fibrosis and orthopedic infections caused by multi drug resistant Gram-negative organisms such as *P. aeruginosa*, *K. pneumoniae*, *A. baumannii* and other extended-spectrum β -lactamase producing gram-negative organisms. Polymyxin is a component of therapy for selective decontamination of the digestive tract, a technique utilized to prevent bloodstream infection and mortality in critically ill patients. Colistin is also useful in the treatment of multi drug resistant infections in cancer neutropenic patients. Synergistic activity against Gram-negative organisms that employ class A β -lactamases of the *Klebsiella pneumoniae* carbapenemase (KPC) type has been reported for the combination of polymyxin B and rifampin. The Gram-negative organisms included in this group are primarily *K. pneumoniae* but include other Enterobacteriaceae, such as other species of *Klebsiella*, *Enterobacter*, *Escherichia*, *Salmonella* and *Citrobacter*.

Polymyxins originally fell from favor due to their toxic properties and poor clinical results. However the emergence of multi-drug resistant Gram-negative organisms and the lack of development of new, effective substances for therapy of such organisms have resulted in the resurgence in use in human medicine. The drugs, however, are almost exclusively “hospital” drugs, used only when absolutely required.

***References available by request. Call the Infectious Disease Epidemiology Section, Office of Public Health, Louisiana Department of Health and Hospitals (504-219-4563)**