Cefazolin: Indications, Dosage, Mechanism of action and side effects

Cefazolin is a semisynthetic first-generation cephalosporin for parenteral administration. Cefazolin has broad-spectrum action due to the inhibition of bacterial cell wall synthesis. It attains high serum levels and its excreted quickly via the urine.

Mechanism of action of cefazolin

In vitro tests demonstrate that the bactericidal action of cephalosporin results from the inhibition of cell wall synthesis. By binding to specific penicillin-binding proteins (PBP) located inside the bacterial cell wall, it inhibits the third and last stage of bacterial cell wall synthesis.

Cell lysis is then mediated by cell wall autolytic enzymes such as autolysins.

Cefazolin sodium for injection is active against the following organisms in vitro and in clinical infections.

- Staphylococcus aureus including penicillinase-producing strains, staphylococcus epidermidis.
- Group A beta-hemolytic streptococci and other strains of streptococci (many strains of enterococci are resistant).
- Streptococcus pneumoniae
- Escherichia coli
- Klebsiella sp
- Proteus mirabilis
- Haemophilus influenza
- Enterobacter aerogenes

Most strains of indole positive proteus (proteus vulgaris), Enterobacter cloacae, morganella morganii and providentia rettgeri are resistant.

Methicillin-resistant staphylococci, Serratia, Pseudomonas, and Acinetobacter calcoaceticus. (Formerly known as Mima and Herella sp) are most uniformly resistant to cefazolin.

Disc-susceptibility-tests-qualitative methods that require measurement of zone diameters give the most precise estimates of antibiotic susceptibility. One such procedure has been recommended for use with discs for testing susceptibility of cefazolin.

With this procedure, a **report** from the laboratory about susceptible indicates that the infecting organisms are more likely to respond to the therapy.

A **report of resistance** indicates that the infecting organisms are not likely to respond to the therapy.

A **report of moderately susceptible** suggests that the organism would be susceptible if the high

dosage is used or if the infection was confirmed to tissues and fluids (eg urine) in which high antibiotic levels are attained.

For gram-positive isolates, a zone of 18 mm is indicative of cefazolin susceptible organism when tested with either the cephalosporin class disc (30 mcg cephalothin) or the cefazolin disc (30 mcg cefazolin).

Gram-negative organisms should be tested with the cefazolin disc (using the above criteria) because cefazolin has been shown by In vitro tests to have activity against certain strains or Enterobacteriaceae found to be resistant when tested with the cephalothin disc. When using the cephalothin disc, gram-negative organisms with zone diameters=18 mm may be considered susceptible to cefazolin; however, organisms with zone diameters less than 18mm are not necessarily resistant or moderately susceptible to cefazolin.

The cefazolin disc should not be used for testing susceptibility to other cephalosporins.

Dilution techniques—A bacterial isolate should be considered susceptible if the minimal inhibitory concentration (MIC) for cefazolin is =16mcg/mL.

organisms are considered resistant if the MIC is=64mcg/Ml.

Pharmacokinetics

Clinical pharmacology studies in patients hospitalized with infections indicate that cefazolin produces peak serum levels approximately to those equivalent to those seen in normal volunteers.

In a study (using volunteers) of constant intravenous infusions with dosages of 3.5mg/kg for 1 hour (approximately 250mg) and 1.5 mg/kg for the next 2 hours (approximately 100mg), cefazolin produced a steady serum level at the third hour of approximately 28mcg/Ml. The average serum concentrations after IV injection of a single 1g dose: average half-life was 1.4 hours.

Controlled studies in adult normal volunteers receiving 1 gram four times a day for 10 days, monitoring CBC, AST, ALT bilirubin, alkaline phosphate, BUN, creatinine, and urinalysis indicated no significant changes attributed to cefazolin.

Cefazolin is excreted unchanged in the urine primarily by glomerular filtration and to a lesser degree by tubular secretion. Following intramuscular injection of 500 mg, 56% to 89% of the administered dosage is recovered within 6 hours, and 80% to nearly 100% in 24 hours.

Cefazolin achieves peak urine concentrations greater than 1000mcg/Ml and 4000mcg/mL respectively following 500mg and 1 gram intramuscular doses. In patients undergoing peritoneal dialysis (2L/hr) mean serum levels of cefazolin were approximately 10-30 mcg/Ml after 24 hours of instillation of a dialyzing solution containing 50mcg/Ml and 72 mcg/Ml (26-142 mcg/mL) WITH 150 MCG/Ml.

Intraperitoneal administration of cefazolin is usually well tolerated. When cefazolin is administered to patients with obstructed biliary tracts, high concentrations well above serum levels occur in the gallbladder tissues and bile. In the presence of obstruction, however, the concentration of the serum antibiotic is considerably lower in bile than the serum.

Cefazolin readily crosses the inflamed synovial membrane and the concentration of the antibiotic achieved in joint space is comparable to levels measured in the serum. Cefazolin readily crosses the placental barrier into the cord blood and amniotic fluid. It is present in very low concentrations on the milk of breastfeeding mothers.

Indication of cefazolin

Cefazolin 1 gram injection is indicated in the treatment of the following infections when due to susceptible microorganisms.

Respiratory tract infections such as tonsillitis, pharyngitis, pneumonia, bronchitis, pulmonary abscess, empyema, pleurisy, sinusitis, laryngitis, and otitis media.

Skin, soft tissue infections, and post-operative infections

Lymphangitis, abscesses, cellulitis, decubitus ulcers, mastitis,(surgical procedures should be performed where included).

Gastrointestinal tract infections

Cholangitis, cholecystitis

Genitourinary tract infections

Pyelonephritis, cystitis, and adnexitis.

Other infections such as bacteremia, septicemia, endocarditis, osteomyelitis, peritonitis, puerperal sepsis.

Contraindications

Patients with hypersensitivity to cephalosporins and their derivatives or any components of their formulations.

Warnings and precautions

Before cefazolin sodium for injection is instituted, a careful inquiry should be made concerning previous hypersensitivity reactions to cephalosporins and penicillins.

Cephalosporin c derivatives should be given cautiously to penicillin-sensitive patients. Serious acute hypersensitivity reactions may require adrenaline and other emergency measures.

There is some clinical and laboratory evidence of partial cross-allergenicity between penicillins and cephalosporins. Patients have been reported to have severe reactions including anaphylaxis to both the classes.

Antibiotics including cefazolin sodium for injection should be administered cautiously to any patient who has demonstrated some form of allergy, particularly to any drugs.

Pseudomembranous colitis has also been demonstrated virtually all broad-spectrum antibiotics such as macrolides, semisynthetic penicillins, and cephalosporins; therefore it's important to consider the diagnosis in patients who develop diarrhea in association with the use of antibiotics. Such colitis may range in severity from mild to life-threatening.

In moderate to severe cases, appropriate measures should be taken. Usage in infants; safety for use in premature and infants under one month of age has not been established.

General precautions

If an allergic reaction to cefazolin occurs, the medicines should be discontinued and the patient treated with the usual agents eg adrenaline and other pressoramines, antihistamines, or corticosteroids. Prolonged use of cefazolin sodium injection may lead to the overgrowth of nonsusceptible organisms.

Careful clinical observation of the patient is critical.

If superinfection occurs during the therapy, appropriate measures should be taken. When cefazolin sodium for injection is administered to patients with low urinary output because of impaired renal function, a lower dosage is required.

The intrathecal administration of cefazolin sodium for injection is not an approved route of administration for this antibiotic. In fact, there have been reports of severe central venous system toxicity including seizures when cefazolin sodium for injection was administered in this manner.

Broad-spectrum antibiotics should be cautiously prescribed for patients with a history of gastrointestinal disease, particularly colitis.

Carcinogenesis, mutagenesis, and impairment of fertility

Mutagenicity studies and long terms studies in animals to determine the carcinogenic potential of cefazolin sodium for injection have not been performed.

Usage In pregnancy

Preproduction studies have been performed in rats given doses of 500 mg or 1 gram of cefazolin sodium for injection/kg and have revealed no evidence of impaired fertility or harm to the fetus due to cefazolin sodium for injection.

There are however no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this medicine should be used during pregnancy only if clearly needed.