Pazufloxacin

Agam Vora

Pazufloxacin is a fused tricyclic quinolone derivative with a 1-aminocyclopropyl substituent at C10 position. The presence of aminoacyl group at C-10 is a unique feature of the molecule imparting potent broad spectrum activity against gram-positive and gram-negative bacteria including variety of resistant strains and anaerobic bacteria.1,2

Mechanism of Action

Pazufloxacin has shown multimodal mechanism of action and inhibits both DNA gyrase and topoisomerase IV enzyme, leading to increased antibacterial spectrum. Moreover, pazufloxacin has been shown to have DNA antagonistic actions also.3 The multimodal mechanism of action is linked to the low potential for the development of resistance in pazufloxacin. Moreover, it has been shown that pazufloxacin is not affected by efflux mechanism of resistance.1,2,4

Spectrum

Pazufloxacin has good antibacterial activity against variety of clinical isolates. The MICs at which 90% of the isolates were inhibited (MIC90s) of pazufloxacin were 0.2 to 0.39 μg/ml for Staphylococcus aureus and Staphylococcus epidermidis, including methicillin-resistant strains.2 Pazufloxacin has similar or 2-fold greater activity than other quinolones, against the following Enterobacteriaceae (MIC90 ≤ 0.25 μg/ml): Escherichia coli, Klebsiella, Enterobacter, Hafnia, Citrobacter, Proteus, Providencia, Serratia, Shigella, Salmonella, Aeromonas and Yersinia. Against P. aeruginosa, pazufloxacin shows more potent activity than tosufloxacin, norfloxacin and ofloxacin. Against clinical isolates of methicillin-resistant Staphylococcus aureus and P. aeruginosa, pazufloxacin has an MIC90 of 0.39 μg/ml and an MIC90 of 0.78 μg/ml respectively. MIC90 for clinical isolates of H. influenzae is ≤ 0.013 μg/l.5

The antibacterial activities of PZFX are superior to those of ceftazidime (CAZ), ceftriaxone, Imipenem/cilastatin (IPM/CS), meropenem against6

- Methicillin resistant S. aureus (MRSA)
- Ampicillin-resistant Haemophilus influenzae,
- ESBL possessing Klebsiella pneumoniae
- Imipenem/cilastatin (IPM/CS)-resistant Pseudomonas aeruginosa

Pharmacokinetics

Pazufloxacin has a Cmax and Tmax of 11.0 ± 2.4 μg/ml attained at 30 min. It is widely distributed in phlegm, lungs, biliary tract, pleural fluid and peritoneal fluid, genital organs and CSF in adequate concentrations. It has a terminal half-life of 1.65 -1.88 hours. Pazufloxacin is predominantly excreted unchanged by the urinary route with the 24-hour urinary excretion being 89.5-93.8% irrespective of dose.

Place in therapy

It may be used as the drug of choice in community acquired infections in unhealthy lung, acute exacerbation of chronic bronchitis and in sepsis following abdominal infections with satisfactory results. Its activity against gram +ve organisms including MRSA and gram – ve organisms including Pseudomonas, Enterobacter and Klebsiella makes it the convenient choice for empirical therapy for unknown infections specially hospital acquired till the culture sensitivity reports are made available.

Indications

Pazufloxacin mesylate I.V. infusion is indicated for the following infections caused by susceptible microorganisms:

- RTIs like pneumonia and lung abscess
- UTIs like cystitis, pyelonephritis and prostatitis
- Abdominal infections like peritonitis, cholecystitis, liver abscess and other intra-abdominal abscesses
- Genital infections like endometritis
- Secondary infections after injuries, burns and post-operative

The current available data does not support its use against atypical infections, though there are a few papers on its use in Legionella infection.

Precaution and Contraindication

Pazufloxacin should be administered with caution to any patient who has a previous history of hypersensitivity for quinolone antimicrobial drugs, patients with severe renal damage, patients who have convulsive disorders such as epilepsy, and elderly patients.

Pazufloxacin is contraindicated in the patients who have a history of hypersensitivity to any component of the formulation, pregnant women, infants and children.

Adverse effects

The most commonly encountered adverse events reported with Pazufloxacin include diarrhoea, rashes, nausea and vomiting. There are case reports of convulsions with the use of the molecule.

Dosage and administration

The usually recommended dose of Pazufloxacin Injections in most infections is 500 mg twice a day administered as an I.V. infusion over 30-60 minutes. Depending on age, symptoms and severity of infection, the dose of the drug may be reduced to 300 mg twice a day.

The total duration of therapy with the drug should not exceed 14 days.

The dose of the drug needs to be modified in patients with moderate to severe renal failure. The maximum recommended dose of the drug should be 300 mg twice a day in such patients.

Asst. Hon. Chest Physician, Dept of Chest and TB, Dr RN Cooper Municipal Gen Hospital, Mumbai.
Limitations

There is inadequate data available that supports its use for atypical infections and currently this drug is available only in injectable form to be used by IV route only. Dose adjustments needs to be done in renal failure patients as convulsions may limit its use.

References


