Cefixime

A Review of its Therapeutic Efficacy in Lower Respiratory Tract Infections

Anthony Markham and Rex N. Brogden

Adis International Limited, Auckland, New Zealand

Various sections of the manuscript reviewed by:

C. Carbon, Service de Médecine Interne, C.H.U. Bichat Claude Bernard, Paris, France; R. Cogo, Department of Pneumology, Ornago Hospital, Milan, Italy; B.I. Davies, Department of Medical Microbiology, De Wever Ziekenhuis, Heerlen, The Netherlands; R.G. Finch, Department of Microbial Diseases, Nottingham City Hospital, Nottingham, England; R.F. Grossman, Division of Respiratory Medicine, Mount Sinai Hospital, Toronto, Ontario, Canada; J.M.T. Hamilton-Miller, Department of Medical Microbiology, Royal Free Hospital, London, England; F.V.P. Maessen, Department of Medical Microbiology, De Wever Ziekenhuis, Heerlen, The Netherlands; Y. Ohsaki, First Department of Internal Medicine, Asahikawa Medical College, Nishikagura, Asahikawa, Japan; J.A. Ramirez, Division of Infectious Diseases, School of Medicine, University of Louisville, Louisville, Kentucky, USA; E. Vogel, Medizinische Klinik III, Kliniken des Main-Taunus-Kreises, Hofheim am Taunus, Germany; R. Wise, Department of Medical Microbiology, City Hospital NHS Trust, Birmingham, England; S.F. Yeo, Department of Medical Microbiology, The London Hospital Medical College, University of London, London, England.

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Summary

Synopsis

Cefixime is an orally active third generation cephalosporin with in vitro antibacterial activity against most important lower respiratory pathogens. The drug is active against Haemophilus influenzae, Moraxella catarrhalis and penicillin-susceptible Streptococcus pneumoniae but not Staphylococcus aureus.
Cefixime has a long elimination half-life (3 hours compared with 0.5 hours for cefaclor and 1.5 hours for cefalexin), which allows once daily administration. Several trials have established the clinical efficacy of the drug in patients with lower respiratory tract infection (LRTI). In comparative studies cefixime had similar efficacy to amoxicillin ± clavulanic acid, cefaclor, cefalexin, cefuroxime axetil and clarithromycin.

Trials evaluating the efficacy of cefixime as the oral component of intravenous to oral switch therapy have produced promising preliminary results although further carefully designed trials are needed in this area.

As with certain other drugs of its class, gastrointestinal disturbances are the most frequently reported adverse events in patients taking cefixime and cases of pseudomembranous colitis have been reported.

Thus, cefixime is an effective treatment for mild to moderate LRTI and may have a role as the oral component of intravenous to oral switch therapy although further well designed studies are needed to confirm initial favourable results in this important emerging area of antibacterial therapy.

Cefixime has good (MIC ≤0.75 mg/L) in vitro activity against *Haemophilus influenzae*, *Moraxella catarrhalis* and penicillin-susceptible (but not penicillin-resistant) *Streptococcus pneumoniae*, the most common lower respiratory pathogens. Certain acute pneumonia pathogens are susceptible to cefixime including *Escherichia coli* and *Klebsiella pneumoniae*, while others, including *Bacteroides* spp., *Peptostreptococcus* spp., *Enterobacter* spp., *Pseudomonas aeruginosa*, *Legionella* spp. and *Staphylococcus aureus* are not.

Oral administration of cefixime 200mg produces peak plasma concentrations of approximately 2.0 to 2.6 mg/L after 3 to 4 hours. Time to maximal plasma concentrations is lengthened slightly when the drug is given with food. Accumulation did not occur after administration of cefixime 400 mg/day for 15 days to volunteers. Cefixime does not appear to penetrate well into sputum but reaches useful levels in bronchial mucosa (up to 2.4 mg/L). Total systemic clearance was 4.4 L/hour (73 ml/min) after administration of a single 200mg intravenous dose of cefixime to volunteers; renal clearance accounted for 40% of this. Clearance was 9.7 L/h (162 ml/min) after oral administration of a single 200mg dose and 11.4 L/h (190 ml/min) after oral administration of a single 400mg dose. Up to 20% of a 200mg dose is recovered unchanged from the urine over a 24-hour period.

Although maximum plasma concentrations and the area under the plasma concentration versus time curve may be greater in older versus younger patients, the dosage of cefixime does not need to be adjusted according to age. However, elimination half-life and clearance are prolonged in patients with severe renal function impairment and in patients on haemodialysis or continuous ambulatory peritoneal dialysis.

Numerous noncomparative and comparative trials have evaluated the efficacy of cefixime as treatment for lower respiratory tract infection (LRTI). In a large noncomparative multicentre trial in patients with acute bronchitis or acute exacerbations of chronic bronchitis, cefixime produced a clinical cure/improvement rate of 96%. The drug has also shown similar efficacy to amoxicillin/clavulanic acid, cefaclor, cefalexin and cefuroxime axetil in patients with various LRTIs.

Studies conducted solely in patients with community-acquired LRTI have also shown cefixime to be clinically efficacious. Comparative studies in this indication...