Antimicrobial Activity, Pharmacokinetics and Clinical Use of Roxithromycin
An Overview

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Summary

Roxithromycin is an orally administered erythromycin derivative that has improved absorption, bioavailability, tolerability and clinical efficacy compared with the parent drug.

Roxithromycin has similar antimicrobial activity to erythromycin, including activity against Mycoplasma pneumoniae, Haemophilus influenzae, Legionella pneumophila, Streptococcus pyogenes, Neisseria meningitidis, N. gonorrhoeae, Corynebacterium diphtheriae, Bordetella pertussis, Branhamella (Moraxella) catarrhalis and Chlamydia trachomatis.

Roxithromycin has excellent enteral absorption and a long serum elimination half-life, and achieves high concentrations in most tissues and body fluids. This favourable pharmacokinetic profile, together with its spectrum of antibacterial activity and good tolerability, makes the drug an efficient agent for the treatment of virtually all respiratory tract infections. Roxithromycin has activity in infections of the genitourinary tract, skin and mouth, and can be used as prophylaxis of bacterial endocarditis.

Thus, roxithromycin has many characteristics making it a useful treatment for community-acquired infections.

Roxithromycin is a recently developed macrolide antibacterial agent. The first macrolide, erythromycin, was developed in 1950 and has been widely used in clinical practice.

Erythromycin is generally recognised to be a safe and effective antibacterial agent. However, it decomposes in acidic conditions to an 8,9-anhydro-6,9 hemiketal and then to a 6,9; 9,12-spirochaetal; since neither of these degradation products has antibacterial activity and the 8,9-anhydro-6,9 hemiketal is reputed to be the cause of many of the gastrointestinal adverse effects of erythromycin, acid-stable alternatives have been sought (see review by Kirst & Sides 1989).

Roxithromycin is a derivative of erythromycin in which the central lactone ring has been stabilised by substituting an ethyl-oxime group for the ketone at C9 (fig. 1; Kirst & Sides 1989). This structural modification of the erythromycin molecule confers better absorption, bioavailability, tolerability and clinical efficacy on roxithromycin.

1. Antibacterial Activity

As reviewed by Young et al. (1989), roxithromycin has an in vitro antibacterial profile that includes activity against Chlamydia trachomatis, Mycoplasma pneumoniae, Branhamella (Moraxella) catarrhalis, Legionella pneumophila and a range of Gram-positive, Gram-negative and anaerobic bacteria responsible for respiratory,
2. Pharmacokinetic Properties

Pharmacokinetic characteristics of roxithromycin that render the drug suitable for use in the treatment of respiratory tract and other infections include a longer half-life than erythromycin and excellent tissue distribution.

Peak serum roxithromycin concentrations (C\textsubscript{max}) of 6.6 to 7.9 and 9.1 to 10.8 mg/L are achieved after oral administration of single doses of 150 and 300mg, respectively, in healthy volunteers (Young et al. 1989). This compares with a C\textsubscript{max} of 1.8 mg/L after the administration of a single 500mg dose of erythromycin stearate in healthy volunteers. C\textsubscript{max} was achieved after a mean of 1.5 to 1.9 hours after oral roxithromycin administration, and area under the serum concentration-time curve (AUC) values ranged between 72.6 and 81 mg/L \cdot h after a single 150mg dose and between 116.5 and 132 mg/L \cdot h after a single 300mg dose (Young et al. 1989).

One of the most marked differences between roxithromycin and erythromycin is in their serum elimination half-lives, with erythromycin having a serum elimination half-life of 1.6 hours (Kavi et al. 1988), compared with 13.2 hours for roxithromycin (Wise et al. 1987).

2.1 Distribution

Macrolides are recognised to have excellent tissue and body fluid penetration (see review by Auckenthaler et al. 1988). Plasma, tissue and body