Pharmacokinetics of a Single Oral Dose of Lomefloxacin in Healthy Elderly Volunteers

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Summary
The pharmacokinetics of lomefloxacin 200 and 400mg, administered orally, were examined in 12 healthy elderly (between 65 and 85 years of age) subjects of both sexes. The drug was well tolerated by all subjects at both doses. Mean C max following the 200mg dose was 2.40 mg/L and the mean t max was 0.96 hours. Plasma half-life averaged 8.54 hours. Following the 400mg dose, the mean C max was 4.48 mg/L, the mean t max was 1.31 hours, and the mean plasma half-life was 8.75 hours. Mean urinary excretion rates were highest in the 0 to 4-hour interval after administration for both doses. Mean cumulative urinary excretion, as a percentage of dose, was similar for both doses. Plasma clearance averaged 146.9 ml/min and 143 ml/min for the 200 and 400mg doses, respectively. Renal clearances averaged 100.9 and 84.3 ml/min for the 200 and 400mg doses, respectively. These values were compared to data after single and multiple doses in male volunteers aged 18 to 45. The changes in clearance values observed in our study compared with those in younger subjects were not of sufficient magnitude to warrant reduced dosage in elderly individuals whose renal function is considered adequate for their age.

Lomefloxacin (fig. 1) is a new difluoroquinolone antimicrobial agent effective in vitro against a broad spectrum of Gram-positive and Gram-negative organisms. When compared with other quinolones, it was more potent than pipemidic acid and comparable in efficacy to norfloxacin and ofloxacin (Chin et al. 1988; Wise et al. 1988). Studies in healthy male volunteers using single and multiple doses of lomefloxacin have shown that the drug is rapidly absorbed, shows good dose proportionality and has a half-life between 7 and 8 hours (Morrison et al. 1988; Morrison et al. unpublished data). This pharmacokinetic profile compares very favourably with that of other quinolones.

Comparison of pharmacokinetic profiles of other quinolones in young adult and elderly individuals revealed that the peak plasma concentrations, and the areas under the plasma concentration-time curves were higher in elderly subjects, while total clearance was lower (Ball et al. 1986; Bayer et al. 1987; Dobbs et al. 1987; Lebel & Bergeron 1987). These differences may be attributable to diminished renal function in the elderly, or to a de-
creased volume of distribution resulting from a lower percentage of body water in the elderly (Shock et al. 1963).

Alteration in the pharmacokinetic parameters of a drug when given to elderly patients may necessitate dosage adjustment in this group. Such a recommendation is made for norfloxacin for elderly patients with reduced renal function (Editorial 1988). The objective of this open-label study was to examine the pharmacokinetics of 2 different single oral doses of lomefloxacin (200 and 400mg) in healthy elderly volunteers.

**Materials and Methods**

**Subjects**

12 healthy volunteers, 9 women and 3 men, with a mean age of 72 years (range 65 to 85) participated in this study after giving written informed consent. A screening evaluation was conducted before the start of the study to verify that each subject was in good health. Study participation was proscribed for individuals with diabetes, cancer, acute dermatitis or active skin lesions, acute gastrointestinal symptoms, a significant infection or known inflammatory process, any clinically significant cardiac, respiratory, metabolic, renal, hepatic, gastrointestinal, immunological, ophthalmological or psychiatric diseases or disorders, a personal or family history of epilepsy or syncope, alcohol abuse or excessive tobacco use. In addition, volunteers were excluded if they had taken antacids within 7 days of beginning the study, were undergoing treatment with any medication, including over-the-counter drugs, had received any medication within 7 days or a regular course of medication within 4 weeks of starting the study, or were known or suspected of having a sensitivity to quinolones or nalidixic acid. The protocol for this study was approved by the Bromley Health Authority Ethical Committee.

**Study Procedures**

Study participants fasted from the evening prior to entry to the test facility until 4 hours after drug administration the following morning. They then received a single 200mg dose of lomefloxacin with 200ml of water on the morning of day 1 after arrival at the clinic; an additional 200ml of water was taken 2 hours later, and fluid intake was then restricted until 4 hours after drug administration. 14 hours postdose the volunteers were released with instructions to return the next morning. After a 14 day washout these procedures were repeated with a 400mg dose of lomefloxacin.

**Safety Monitoring**

The tests used to determine subject eligibility, including vital signs measurement (standing and supine blood pressures, radial pulse and respiratory rate) were repeated before drug administration.

**Sampling Procedures**

Baseline blood samples were collected by venepuncture for lomefloxacin assay before the first dose of lomefloxacin, with the volunteers in the fasting state, and at 0, 0.33, 0.66, 1, 1.5, 2, 2.5, 3, 4, 6, 8, 10, 12, 14, 24, 38 and 48 hours after drug administration. Plasma was separated from whole blood and stored at -20°C until assayed.

Urine was collected before and over the intervals 0, 0 to 4, 4 to 8, 8 to 14 and 14 to 24 hours after administration. The volume collected was recorded and an aliquot frozen at -20°C for analysis. Small fresh urine samples were also collected within the 0 to 4-hour and 4 to 8-hour intervals for microscopic examination for lomefloxacin crystals.

**Lomefloxacin Assay**

Lomefloxacin concentrations in plasma and urine were determined by high performance liquid chromatography (HPLC) [Okezaki et al. 1988]. Briefly, samples were extracted into chloroform-isoamyl alcohol (19 : 1 v/v) at pH 7.0 and evaporated. The residue was dissolved in the mobile phase (acetonitrile, citric acid 0.05 mol/L, ammonium acetate 1.0 mol/L; 22 : 77 : 1) and analysed on a reverse-phase column (Nucleosil C-18,