Tissue penetration of a single dose of levofloxacin intravenously for antibiotic prophylaxis in lung surgery

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Sir,

Levofloxacin has proved its in vivo efficacy in numerous clinical trials of community- and hospital-acquired respiratory infections. In this study, levofloxacin concentrations in serum and lung tissue were determined by HPLC after a single 500 mg iv dose, given as perioperative prophylaxis to six patients undergoing lobectomy or pulmonary segment resection. The study was approved by the ethics committee of Heidelberg University and written consent was obtained from all patients.

A single dose of 500 mg levofloxacin (Aventis, Bad Soden, Germany) was administered as an intravenous infusion. Duration of infusion was 30, 40, 45 (twice), 50 and 60 min. Lung tissue specimens and blood samples were taken simultaneously 90 min (median value) post-dosing. Serum and lung samples were stored at –30°C until assayed. The samples were prepared by protein precipitation with acids and methanol; this yielded high recoveries (for serum 98% and lung 90%). The compounds were separated on a reversed phase column with an acidic mobile phase containing triethylamine. The eluate was monitored by fluorescence detection. The HPLC assay is linear over the usable concentration range (0.1–40 mg/L) and it provides good validation data for accuracy and precision. The interday coefficients of variations ranged for serum and lung tissue from 4.0 to 5.3% and from 2.1 to 6.5%, respectively.

In October 1999, six patients (four male, two female) with a median age of 49 years were entered into the study. The patients' weight ranged from 46 to 94 kg, serum creatinine levels were within the normal range (0.4–0.88 mg/mL). In four patients a malignant tumour had been diagnosed.

Mean serum concentrations of levofloxacin were 6.6 ± 2.7 mg/L; mean tissue concentrations 18.3 ± 7.2 mg/L 90 min post-dosing. The mean tissue:serum ratio was 2.8. A good correlation was seen between serum and tissue levels with a correlation coefficient of 0.8271 (Figure).

The effectiveness of antibiotic prophylaxis with cephalosporins in lung surgery has already been demonstrated in randomized double-blind studies. Most data available about levofloxacin concentrations in lung tissue were determined after oral administration of the drug. In the majority of studies tissue samples had been taken by bronchoscopy. This might explain the lower tissue concentrations (7.7–8.3 mg/L) observed by these authors compared with our data. Comparable with our results, however, are the data published by Wijnands and others after oral application of 600 mg of ofloxacin. Tissue samples were collected intra-operatively and mean tissue concentrations reached 17.7 ± 9.2 mg/L. Measuring whole lung tissue samples might seem of limited value, because they are a mixture of different compartments. However, the investigation of bronchoscopically obtained samples may not reflect the conditions in deep invasive respiratory infections. Thus, lung tissue samples, although only rarely obtained, might provide additional information about these conditions.

In our study, after a single iv dose of levofloxacin, the concentrations measured in tissue and serum exceeded the MIC90s of common respiratory pathogens at least 10-fold. Pharmacokinetic/pharmacodynamic models indicate that for clinical efficacy a peak:MIC ratio of >12.2 is necessary.

Figure. Correlation of levofloxacin levels in serum and lung tissue in six patients 90 min post-dosing with 500 mg levofloxacin iv.

One patient suffered from emphysema and one patient had pulmonary lesions of unknown origin. However, none of the samples investigated was obviously inflamed or infiltrated.
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mg/L) or Moraxella catarrhalis (0.06 mg/L) as well as for most of the Enterobacteriaceae, these ratios are easily reached within 1 h post-dosing.

Thus our results suggest that levofloxacin may be well suited for perioperative prophylaxis in patients undergoing lung surgery.

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References


