Vitreous penetration of levofloxacin in the uninflamed phakic human eye

E N Herbert, I A Pearce, J McGalliard, D Wong, C Groenewald

Aims: To assess the vitreous penetration of oral levofloxacin (a new fluoroquinolone antibiotic with improved Gram positive activity) in uninflamed phakic eyes.

Methods: 15 patients for macula hole surgery were recruited to the study. 10 received a single 500 mg dose of levofloxacin by mouth preoperatively. Five acted as controls. Serum and undiluted vitreous samples were obtained at surgery and analysed by HPLC.

Results: Levofloxacin was detectable 2.5 hours after administration in the vitreous. A peak concentration of 1.6 µg/ml (or mg/l) was measured between 2.5 and 4 hours post-dose.

Conclusion: Oral levofloxacin reaches the vitreous rapidly in the uninflamed phakic eye. Levels did not reach the MIC90 for the commonest infecting organisms. Nevertheless, levofloxacin would be expected to be active against a higher proportion of infecting organisms than either ciprofloxacin or ofloxacin.

RESULTS

Fifteen patients were recruited. Of the 10 receiving levofloxacin seven were female, three male. Mean age was 65 (range 46–76) and mean weight was 70 kg (range 57–100 kg). All were phakic. Seven had surgery under local anaesthesia with no preoperative fasting; three had a general anaesthetic with 6 hours’ fasting. Vitreous samples were collected, on average, 20 minutes (range 15–40 minutes) after the serum samples. Levels of levofloxacin achieved are shown in Figure 1. Levofloxacin was detectable in the serum of all treated patients, the earliest being taken only 55 minutes after administration (range 3.0–6.9 µg/ml). The range of vitreous levels was 0.0–1.6 µg/ml. No levofloxacin was found in the serum or vitreous of control cases. No adverse drug reactions were noted.

DISCUSSION

The fluoroquinolones have high oral availability, approximately 99% for levofloxacin, and are absorbed rapidly. Food does not significantly affect absorption. Maximum serum concentrations are achieved after 1 hour when fasted or 2 hours unfasted. Our results are consistent with this rapid availability in serum. We have found that levofloxacin reaches the vitreous of uninflamed phakic eyes within 2.5 hours of a single oral dose. The peak concentration measured (1.6 µg/ml) was less than half the highest reported MIC90 for Staphylococcus epidermidis, the commonest organism isolated in post-cataract
endophthalmitis (Table 1). It is well recognised that sensitivities to most antibiotics for *S. epidermidis* are very variable (as seen by the large range in Table 1) and resistance widespread. The MIC90 values quoted may not be representative of organisms encountered in endophthalmitis as they include isolates obtained from blood cultures in cancer patients, many of whom had received recent antimicrobial therapy. 

### Table 1 MIC90 values for organisms commonly isolated in bacterial endophthalmitis. Values in µg/ml

<table>
<thead>
<tr>
<th>Organism</th>
<th>% isolates in EVS</th>
<th>Highest MIC90</th>
<th>Ref 8, 1999</th>
<th>Ref 9, 1997</th>
<th>Ref 11, 1994</th>
<th>Ref 12, 1998 (MIC90)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus epidermidis</td>
<td>70</td>
<td>4.0 (16.0)</td>
<td>4.0</td>
<td>4.0 (16.0)</td>
<td>0.42</td>
<td>0.25-0.41</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>9.9</td>
<td>0.5 (16.0)</td>
<td>0.25</td>
<td>0.25 (8.0)</td>
<td>0.41 (0.52)</td>
<td>0.25-0.5 (0.05-16)</td>
</tr>
<tr>
<td>Streptococcus viridans</td>
<td>3.7</td>
<td>2.0</td>
<td>2.0</td>
<td>1.91</td>
<td>0.06-2.0</td>
<td></td>
</tr>
<tr>
<td>Streptococcus pneumoniae*</td>
<td>2.2</td>
<td>2.0</td>
<td>2.0</td>
<td>1.89</td>
<td>1.0-3.13</td>
<td></td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>1.2</td>
<td>3.13</td>
<td>2.0</td>
<td>2.0</td>
<td>1.91</td>
<td></td>
</tr>
<tr>
<td>Bacillus cereus†</td>
<td>0.3</td>
<td>2.0</td>
<td>0.25</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>1.9</td>
<td>0.25</td>
<td>0.25</td>
<td>0.18</td>
<td>0.06-0.25</td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae*</td>
<td>0.05</td>
<td>0.05</td>
<td>0.03</td>
<td>0.02</td>
<td>0.015-0.05</td>
<td></td>
</tr>
</tbody>
</table>

MIC90 is the minimum concentration of antibiotic required to inhibit replication in 90% of clinical isolates in vitro. Figures in parentheses are for methicillin resistant organisms.

*More common in late post trabeculectomy endophthalmitis; †more common in post-traumatic endophthalmitis.

In vitro testing of antibiotic susceptibilities does not relate precisely to in vivo response. Infections due to apparently resistant organisms may respond and, conversely, treatment may fail in susceptible infections, yet it remains the most practical guide available. It is likely that MIC values will rise as resistance becomes more widespread. This has been seen for other fluoroquinolones tested on isolates from bacterial keratitis. Discretion should be used to reduce inappropriate use of these antibiotics and limit spread of resistance.

The role of systemic antibiotics in therapy or as prevention for endophthalmitis has not been established. Direct intravitreal treatment remains the mainstay of treatment. Systemic agents with adequate vitreous penetration and an appropriate antimicrobial spectrum may have a valuable role. The penetration of levofloxacin and newer fluoroquinolones into the infected eye and their effect on outcome require further investigation.

**ACKNOWLEDGEMENTS**

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