Chemotherapy of Otitis Media with Ofloxacin

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Summary

This study evaluated the therapeutic role of ofloxacin in different forms of otitis media. After identifying the infecting bacteria in 250 patients with acute otitis media, or chronic otitis media, the clinical efficacy of orally administered ofloxacin 200mg twice daily was assessed in 45 patients from each of these groups. The clinical results were comparable with those obtained after conventional local and oral antibiotic therapy. Microbiological examination of the ear secretions revealed Staphylococcus aureus, Streptococcus pyogenes, Streptococcus pneumoniae and Haemophilus influenzae to be the main pathogens in acute otitis media, whereas in chronic otitis media P. aeruginosa and Proteus sp. were detected in most of the cases. Ofloxacin concentrations in secretions and mucosa specimens of the middle ear exceeded serum concentrations by more than 2-fold. On the basis of these preliminary results, ofloxacin appears to be an effective orally administered agent, without ototoxicity, which is effective against S. aureus and P. aeruginosa, 2 important pathogens in middle ear infections. Ofloxacin should be considered as an alternative for the therapy of otitis media, especially the chronic forms.

In nearly all cases of acute, as well as chronic, otitis media, infecting bacteria can be identified and quantified by means of microbiological examination. For proper antibacterial chemotherapy and the clinical evaluation of new antibiotics, acute and chronic forms of otitis media have to be distinguished because the bacterial spectra and clinical features show important differences. In addition, the fluid and mucosal concentrations of the antibiotic drug should be much higher than the minimum inhibitory concentrations (MIC), which must be low for the relevant bacteria, and there should be no potential risk of ototoxicity. However, proper clinical evaluation of a new agent demands a comparison of the clinical results with those of routine management with oral penicillin for acute otitis and combined local/oral antibiotic therapy, as well as middle ear surgery, for the chronic forms.

Considering these points, the following study was performed to evaluate the clinical efficacy and safety of ofloxacin in middle ear infections. The data accompany and expand on results previously reported (Lenarz 1986a,b).

1. Materials and Methods
1.1 Characteristics of Otitis Media

Acute otitis media is characterised by an acute onset of pain, hearing loss and sometimes secretion following perforation of the tympanic membrane.
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in 1 or both ears. The disease is self-limiting, normally lasting for 7 to 10 days. Its duration is usually assessed as the time required for normalisation of the ear drum and hearing. Chronic forms of otitis media are characterised by recurrent fluid secretion and permanent conductive hearing loss due to perforation of the tympanic membrane and damage to the ossicular chain. Diagnosis was made by otoscopic examination and microscopy. Fluid specimens were taken from the outer ear canal and mucosal specimens were taken through perforations of the ear drum.

1.2 Microbiology

In 65 cases of acute otitis media, 88 of otitis media chronica mesotympanalis and 97 of otitis media chronica epitympanalis, the infecting organisms in middle ear secretions were ascertained by use of culture methods. Sensitivities to ofloxacin were determined by the agar diffusion test.

1.3 Treatment Schedule

45 patients from each group with acute otitis media, otitis media chronica mesotympanalis and otitis media chronica epitympanalis were treated with ofloxacin 200mg twice daily for 7 to 20 days. After 2 days of treatment, a sample of secretion or a specimen of middle ear mucosa was taken simultaneously with a sample of venous blood for determination of drug levels. The results were compared with those of conventional local and oral antibiotic treatment; namely, ear drops containing chloramphenicol, tetracyclines or aminoglycosides and oral penicillin.

1.4 High Performance Liquid Chromatography Analysis

The ofloxacin concentrations in middle ear mucosa, middle ear secretion and plasma were determined by high performance liquid chromatography (HPLC) [Verho et al. 1985] in 12 patients (4 from each group) 2 hours after the last oral dose of 200mg.

2. Results

2.1 Bacteriology

The bacterial pathogens identified in the several forms of otitis media and the proportions susceptible to ofloxacin are shown in table I. *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae* and *Haemophilus influenzae* were the predominant bacteria in acute otitis media, whereas *Pseudomonas aeruginosa* and *Proteus* sp. were most frequently identified in otitis media chronica.

<table>
<thead>
<tr>
<th>Bacterial Pathogens</th>
<th>AO (n = 65)</th>
<th>OCM (n = 88)</th>
<th>OCE (n = 97)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>19/95/0.21</td>
<td>32/88/0.33</td>
<td>25/90/0.26</td>
</tr>
<tr>
<td><em>Streptococcus pyogenes</em></td>
<td>33/85/0.91</td>
<td>18/91/1.23</td>
<td>9/100/1.17</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>35/97/0.45</td>
<td>47/93</td>
<td>2/100</td>
</tr>
<tr>
<td><em>Proteus</em> sp.</td>
<td>5/80</td>
<td>58/90</td>
<td></td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>9/85/0.91</td>
<td>37/82/1.38</td>
<td>95/91/1.2</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>28/63</td>
<td>15/100/0.16</td>
<td>9/88/0.17</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>28/63</td>
<td>9/44/2.31</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: no. = number of patients; % = percentage of bacterial strains which are susceptible to ofloxacin; AO = acute otitis media; OCM = otitis media chronica mesotympanalis; OCE = otitis media chronica epitympanalis.