CEREBROSPINAL FLUID AND SERUM AMPICILLIN LEVELS IN BACTERIAL MENINGITIS PATIENTS AFTER INTRAVENOUS AND INTRAMUSCULAR ADMINISTRATION

By

Isis A. Mikhail, John E. Sippel, Nabil I. Girgis and Mohamed W. Yassin

U. S. NAVAL MEDICAL RESEARCH UNIT NO. 3
(CAIRO, ARAB REPUBLIC OF EGYPT)
FPO NEW YORK 09527
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INTRODUCTION
Ampicillin has been shown to reach therapeutically significant levels in cerebrospinal fluid (CSF) and to be effective in the treatment of bacterial meningitis. However, intramuscular (IM) administration was found to simplify management of patients with meningitis, as CSF specimens obtained 1 h after IM administration contained detectable levels of ampicillin in patients with meningococcal meningitis receiving IM or IV ampicillin during the first 2 days of therapy were compared.

RESULTS
The range and mean CSF and serum ampicillin levels are given in Table II. The mean CSF values obtained 1 h after IM or IV administration were comparable on days 1 and 2. However, the mean CSF levels 4 h after administration were significantly higher in the patients who received the drug by the IM route both on day 1 (p < 0.02) and day 2 (p < 0.01). The CSF-serum ratios (× 100) were approximately 5 one hour after ampicillin administration either route on both days. These ratios rose to approximately 50 at 4 h after administration. There was no noticeable difference in the clinical response with IM or IV administration. One patient with meningococcal meningitis died in the IM group, and one patient with meningococcal meningitis died in the IV group.

*The opinions and assertions contained herein are the private ones of the authors and are not to be construed as official or as reflecting the views of the Department of the Navy or the naval service at large.
Table I. Bacterial meningitis patients included in ampicillin study

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Intramuscular</th>
<th>Intravenous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neisseria meningitidis</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Age (range)</td>
<td>5 mo - 20 yr</td>
<td>4 mo - 62 yr</td>
</tr>
<tr>
<td>Age (mean)</td>
<td>7.7 yr</td>
<td>10.5 yr</td>
</tr>
<tr>
<td>Male/female ratio</td>
<td>1.3</td>
<td>0.7</td>
</tr>
</tbody>
</table>

*Patient with Staph. aureus meningitis was given ampicillin IM after 2 days of ampicillin therapy.

DISCUSSION

Little data are available on the ampicillin CSF levels achieved after IM administration. Barrett et al. (1), had mean concentrations of 0.43 μg/ml in normal subjects to 0.65 μg/ml in patients with viral meningitis. Thrupp et al. (6) gave ampicillin IM in patients with purulent meningitis but only after they had responded satisfactorily with IV therapy. In patients with haemophilus meningitis, Wilson and Haltalin (7) demonstrated mean CSF ampicillin levels of 2.0 μg/ml 1 h after an IV dose, 2.1 μg/ml 4 h after an IV dose, 4.7 μg/ml 1 h after an IM dose, and 4.1 μg/ml 4 h after an IM dose during the second day of ampicillin therapy. Their data are consistent with this report, showing that the CSF levels are higher 4 h after IM administration.

IM administration of ampicillin resulted in concentrations higher than the MICs for the usual agents of bacterial meningitis (3, 6, Mikhail et al., unpublished data). IM ampicillin therefore appears to be an effective therapeutic regimen for bacterial meningitis and may be particularly suitable for outbreaks of meningococcal disease in developing countries.

ACKNOWLEDGEMENTS

We thank Dr Michael Kilpatrick for his helpful suggestions regarding this manuscript and Miss Alexandra Patsalidis for its preparation.

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Table II. Cerebrospinal fluid and serum ampicillin levels in bacterial meningitis patients

<table>
<thead>
<tr>
<th>No. of pat.</th>
<th>CSF levels (μg/ml)</th>
<th>Serum levels (μg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
<td>Mean</td>
</tr>
<tr>
<td>Intramuscular route</td>
<td>Day 1</td>
<td>1 h</td>
</tr>
<tr>
<td></td>
<td>4 h</td>
<td>0.44-9.50</td>
</tr>
<tr>
<td></td>
<td>Day 2</td>
<td>1 h</td>
</tr>
<tr>
<td></td>
<td>4 h</td>
<td>0.42-8.40</td>
</tr>
<tr>
<td>Intravenous route</td>
<td>Day 1</td>
<td>1 h</td>
</tr>
<tr>
<td></td>
<td>4 h</td>
<td>0.22-2.90</td>
</tr>
<tr>
<td></td>
<td>Day 2</td>
<td>1 h</td>
</tr>
<tr>
<td></td>
<td>4 h</td>
<td>0.20-1.70</td>
</tr>
</tbody>
</table>

REFERENCES


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#### Author(s)
Isis A. Mikhail, John E. Sippel, Nabil I. Girgis and Mohamed W. Yassin

#### Performing Organization Name and Address
U.S. Naval Medical Research Unit No. 3
FPO New York 09527

#### Controlling Office Name and Address
Naval Medical Research and Development Command
National Naval Medical Center
Bethesda, MD 20814

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#### Abstract
28 patients with bacterial meningitis received ampicillin by the intramuscular (IM) route and 16 patients by the intravenous (IV) route. The mean cerebrospinal fluid (CSF) ampicillin levels were similar in the two groups 1 h after a dose given on the first or second day of treatment, but they were higher in the IM group on both days 4 h after a dose. CSF/serum ratios were similar in both groups but considerably higher at 4 h than at 1 h.

#### Key Words
- Bacterial Meningitis
- Cerebrospinal fluid (CSF)
- CSF/serum ratio