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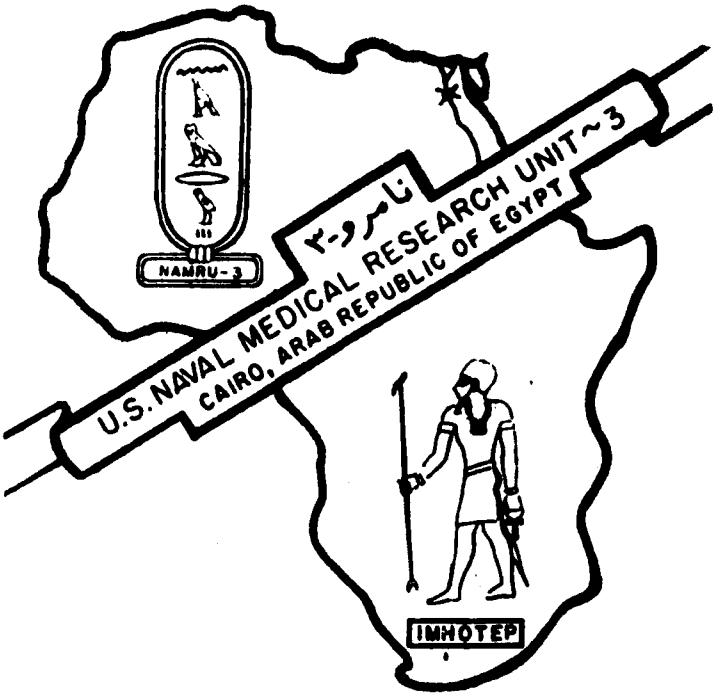

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CEREBROSPINAL FLUID AND SERUM AMPICILLIN LEVELS IN BACTERIAL MENINGITIS PATIENTS AFTER INTRAVENOUS AND INTRAMUSCULAR ADMINISTRATION

By

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Short Communication

Cerebrospinal Fluid and Serum Ampicillin Levels in Bacterial Meningitis Patients after Intravenous and Intramuscular Administration*

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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.

INTRODUCTION

Ampicillin has been shown to reach therapeutically significant levels in cerebrospinal fluid (CSF) (5) and to be effective in the treatment of bacterial meningitis (4, 5) when it is administered intravenously (IV). However, intramuscular (IM) administration would simplify management of patients especially in areas where modern medical facilities are not readily available. Since little has been reported on the CSF levels that can be obtained after IM administration in patients with inflamed meninges, ampicillin concentration in blood and CSF specimens from patients with bacterial meningitis receiving IM or IV ampicillin during the first 2 days of therapy were compared.

PATIENTS AND METHODS

44 patients (Table I), whose admission CSF and serum samples contained no detectable antibiotics, were given 160 mg/kg/day of ampicillin divided into 6 doses at 4-h intervals. The first 10 patients were given the drug by the IM route, after which IM or IV administration was used according to a predesigned randomization table. 28 patients received the drug by the IM route for 5–7 days and 16 patients by the IV route for 2 days followed by IM for 5 days. Both groups were then given oral ampicillin for 1 week. CSF and sera were obtained from 16 patients 1 h after the first dose, 13 patients 4 h after the first dose, 14 patients 1 h after the 7th dose, and 17 patients 4 h after the 7th dose. 16 patients had CSF and sera obtained on both day 1 and day 2 (Table II).

The simplified agar-well diffusion method (2) using Bacillus subtilis spore suspension (Difco Laboratories) was employed in the determination of ampicillin concentrations in the CSF and sera with simultaneous parallel comparison to antibiotic standards ranging from 0.1 to 80.0 μg/ml. The standards and specimens were stored together at −70°C until tested. Each assay involved 3 replicates of the test specimens and standards.

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 by 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 and one patient with meningitis of unknown etiology 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*

	Intramuscular	Intravenous
Etiology		
Neisseria meningitidis	18	9
Streptococcus pneumoniae	4	2
Haemophilus influenzae	1	
Staphylococcus aureus		1[a]
Unknown	5	4
Age (range)	5 mo – 20 yr	4 mo – 62 yr
Age (mean)	7.7 yr	10.5 yr
Male/female ratio	1.3	0.7

[a] Patient with Staph. aureus meningitis was given staphcillin IM after 2 days of ampicillin therapy

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

	No. of pat.	CSF levels (μg/ml) Range	CSF levels (μg/ml) Mean	Serum levels (μg/ml) Range	Serum levels (μg/ml) Mean
Intramuscular route					
Day 1					
1 h	10	0.10–1.65	1.06	10.75–30.50	21.42
4 h	9	0.44–9.50	3.64	<0.10–33.00	8.54
Day 2					
1 h	9	0.23–1.95	1.02	8.00–35.00	19.50
4 h	11	0.42–8.40	2.94	1.60–20.50	7.27
Intravenous route					
Day 1					
1 h	6	0.31–2.50	1.09	10.00–28.50	17.83
4 h	4	0.22–2.90	1.02	0.30–6.00	2.30
Day 2					
1 h	5	0.52–0.82	0.66	1.85–27.00	13.37
4 h	6	0.20–1.70	0.67	0.40–4.50	1.70

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 and 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 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.

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