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Treatment type of 212 cases of community acquired and nosocomial bacterial meningitis

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Abstract

Bacterial meningitis requires early treatment with aggressive use of potent antimicrobials, otherwise the outcome almost ends fatally. This prospective study includes 1442 cases of pyogenic meningitis which have been admitted to the Teaching Fever Hospital/ Neurosurgical Unit in Baghdad over a period of 15 years (1991 – 2006). The diagnostic yield by isolation and culturing of the causative microbes from the CSF was positive for 212 cases (14.7%). The antibiotics used in the treatment of the cases were different and in many instances not practiced according to the standard schedule, but to the availability of the antimicrobial agents during the years of blockade on Iraq between 1990 and 2003. The number of cases was 212 (113 male and 99 female); of these, 170 cases were community acquired and 42 cases were hospital- acquired meningitis in the neurosurgical unit. The age of treated patients ranged between 1-67 years with no significant difference between gender and ages. The pattern of bacteria species isolated from CSF were *S. pneumoniae* (104), *N. meningitis* (44), *H. influenzae* (22), E.coli (14), *Pseudomonas spp.* (8), *Proteos* (8), *S. aureus* (2), *Salmonella* (2) and eight other isolates . The antibiotics used were penicillin, ampicillin, chloremphenicol, cefotaxim, ceftriaxone, rifampicin, gentamycin, tobramycin, and vancomycin singly or in various combinations. The treatment of cases ranged between 1-3 weeks according to type of the microorganism. The case fatality rate (*CFR*) was 12.2% for meningitis caused by *S. pneumoniae*, 5.3% for *N. meningitis* and 4.5% for *H. influenzae*. The CFR for nosocomial meningitis was 28.6%; it was highest among *salmonella* and *S. aureus* cases. It can be concluded that the empirical antibiotic regimens should be evaluated each time to escape the development of antimicrobial resistance; also, longer courses of antibiotic therapy might not be needed.

Key words: *antibiotics, bacterial meningitis, nosocomial meningitis*

Introduction

Bacterial meningitis is a life-threatening illness that results from bacterial infection of the meninges (1-4). Beyond the neonatal period, the 3 most common organisms that cause acute bacterial meningitis are *Streptococcus pneumoniae, Neisseria meningitides,* and *Haemophilus influenzae* type b (Hib)(3-6) . Although *S pneumoniae* was the leading cause of community-acquired bacterial meningitis in the United States, but since the introduction of the conjugate pneumococcal vaccine in 2000, the rate of pneumococcal meningitis in the USA has declined 59% (1, 5-7). The emergence of penicillin-resistant *S pneumoniae* has resulted in new challenges in the treatment of bacterial meningitis (1, 2). Antibiotics should be administered as soon as possible once bacterial meningitis is established in patients (8-13). Initial antibiotic selection should provide coverage for the 3 common pathogens: *S pneumoniae*, *N meningitides*, and *H influenza* (1-5, 14).

The combination of vancomycin with either ceftriaxone or cefotaxime is recommended for those with suspected bacterial meningitis, based upon susceptibilities of isolated pathogens if possible (1, 2, 12, 14).This combination provides adequate coverage for most penicillin-resistant pneumococci and beta-lactamase resistant Hib (1, 2, 13). However, Ceftazidime has poor activity against pneumococci and should not be substituted for cefotaxime or ceftriaxone.

Traditionally, initial antimicrobial treatment consists of ampicillin and an amino glycoside combination (ampicillin and ce-

fotaxime also appropriate), and if *S. pneumoniae* infection is suspected, vancomycin should be added. Initial empiric therapy for late-onset disease in preterm infants should include an antistaphylococcal agent and ceftazidime, amikacin, or meropenem (carbamapenems group). Several third-generation cephalosporins achieve good CSF levels and have emerged as effective agents against gram-negative infections. There has been considerable good experience with use of cefotaxime and ceftriaxone (1, 3, 5). Also, aminoglycosides; gentamicin and tobramycin have proven effective when combined with a beta-lactam antibiotic for the treatment of pediatric cases of meningitis caused by bacteria such as group B streptococci and susceptible enterococci. Routine intrathecal administration of aminoglycosides has no additional benefit in this capacity (1).

Hospital-acquired meningitis caused by *S. aureus,* anaerobic bacteria and *P. aeruginosa* may require other antimicrobials, such as methicillin, oxacillin, vancomycin, or a combination of ceftazidime with amino glycoside for *P. aeruginosa* . The etiologic agent and clinical course will determine the duration of treatment, the guidelines are not standardized and therefore duration of therapy may need to be individualized on the basis of the patient's clinical response.

Vancomycin and rifampin should be considered for infection with *S. pneumoniae*; chloramphenicol is recommended for patients with meningococcal meningitis who have significant hypersensitivity to beta-lactam antimicrobial agents (1-4, 13-17). Examination of the CSF at the end of treatment has not proven helpful in predicting relapses of meningitis (1, 18-20). The study has been done during the period of severe blockade on Iraq, therefore susceptibility test of isolates in vitro was not always available and the study has more concentrated on the bacterial etiology and outcome of treated bacterial meningitis.

Patients and Methods

All cases of pyogenic meningitis over a period of 15 years (1991 – 2006) admitted to the Teaching Fever Hospital - Neurosurgical Unit in Baghdad were studied. The cases were referred from private physicians, other hospitals for diagnosis and treatment or they were admitted directly to the Neurosurgical Unit of the Teaching Hospital for cranial surgery. Thorough clinical and neurological examination was done for each patient besides the following investigations are routinely done: Hematocrit values, CSF examination for chemistry and microbial detection by Gram stain and CSF culture on aerobic and anaerobic culture media. Brain visualization by MRI and CT scan imaging were done when indicated for some patients but not routinely for all cases. On admission, and after CSF specimen taken from patients, an intravenous line is set up and empirical antibiotics treatment is starting depending on the availability of the antibiotic type in hospital. Ampicillin alone or in combination with Chloramphenicol or gentamycin is given. Cases of nosocomial infection were mostly given vancomycin, cefotaxim and ceftriaxone singly or in combination. Rifampicin or tobramycin were added for some cases of *Pseudomonus* and *Proteus* meningitis. The antibiotic might be changed after the CSF results to another more potent one (if it is available) or it was continued to complete the recommended course.

Results

This study includes only patients diagnosed by culture isolation of bacteria from their CSF specimens. These were 212 cases (170 community acquired and 42 hospital acquired). There were 113 males and 99 females; their age ranged between 1-67 years (means 35 years for males and 32 years for females) (**Table 1**). The hospital acquired bacteria species were *14 E.coli, 8 Pseudomonas spp., 8 Proteus spp., and each 2 S. aureus* and *Salmonella spp.* Eight other isolates were included; *Acinetobactor spp., Streptococcus viridians, Listeria spp., Enterococci spp. and Mimma polymorpha* (**Table 2**).

The community acquired cases of meningitis were 170 cases, represented by 104 cases of pneumococcal meningitis, 44 cases of *N. meningitides* and 22 of H.influenzae b (Hib) (**Table 3**). There was no significant difference between the different combinations of antibiotics on the outcome of the CFR of the different cases of the community acquired meningitis, no difference between them according to the gender. There was significant difference ($p < 0.001$) in the CFR between the hospital- acquired and the community acquired types of meningitis.

TABLE 1. Gender and age of cases of bacterial meningitis (No. 212 cases)

Gender	No. of cases	Mean age (years)
Males	113	35 (2-67)
Females	99	32 (1-58)
Total	212	

TABLE 2. Cases of Nosocomial Meningitis (No 42 cases)

Microbial type	Type of Treatment	Number of cases	Case Fatality Rate (CFR)
E.coli	Cefotaxim	6	16.7
	Cefotaxim + Ampicillin	8	12.5
Pseudomonas	Cefotaxim + Gentamycin	4	25
	Cefotaxim + Tobramycin	4	25
Proteos	Cefotaxim + Rifampicin	8	25
S.aureus	Vancomycin	1	50
	Vancomycin + Cefotaxim	1	100
Salmonella	Chlorempheniсol + Cefotaxim	1	100
	Cefotaxim	1	100
Others	Ceftriaxone	8	25
Total		42	28.6

TABLE 3. Types of microorganisms and anti microbial treatment in the community-acquired bacterial meningitis with their CFR, (no. 170 cases)

Type of microorganisms	Number of cases	Types of Treatment	Case Fatality Rate % (CFR)
Streptococcus pneumoniae (104 cases)	40	Ampicillin	11.5
	28	Ampicillin + Chloremphenicol	13.8
	22	Chloremphenicol	14.5
	14	Cefotaxim	7.1
Nisseria meningitides (44 cases)	18	Penicillin	4.2
	16	Chloremphenicol	6.25
	10	Chloremphenicol + Ampicillin	5.8
H. influenzae (22 cases)	4	Amicillin	0
	12	Amicillin + Chloremphenicol	8.33
	6	Cefotaxim	0

Discussion

Prompt administration of antibiotics to a patient with suspected bacterial meningitis is essential for successful cure especially without complication. We used ampicillin "single or in combination" as empirical drug for treatment of nearly 70% of the community-acquired bacterial meningitis. Ampicillin provides good coverage for gram-positive cocci, including group *B streptococci, enterococci, L monocytogenes*, some strains of *E coli*, and *Hib*. Ampicillin also achieves adequate levels in cerebrospinal fluid (CSF)(1, 3, 21-26). Aminoglycosides (amikacin, gentamicin, tobramycin) have good activity against most gram-negative bacilli, including *P. aeruginosa* and *S. marcescens*. However, aminoglycosides achieve only marginal levels in both CSF and ventricular fluid, even when the meninges are inflamed (17, 22). Cephalosporins are empirically given for undiagnosed cases of meningitis elsewhere as recommended in many references (1-4, 18). We used cefotaxim singly for treatment of six cases of *E.coli* meningitis and one case of Salmonella meningitis and the CFR was higher than in its combination with ampicillin (16.7% vs. 12.5% respectively). Cephalosporin's have no any activity against *L. monocytogenes* and *enterococci* and, therefore, should not be used as a single agent for initial treatment especially among hospital-acquired cases. If the bacterial isolate is susceptible in vitro to ampicillin with a low minimum inhibitory concentration (MIC), then ampicillin may be continued used alone (14, 15) . Cefotaxime and ceftriaxone also provide good activity against most penicillin-resistant *S. pneumoniae* (16). This study has used treatment with cefotaxim and ceftriaxone for most hospital-acquired meningitis cases, and only used for minority of the community-acquired cases (12% of *S. pneumoniae* and *Hib*). Both vancomycin and cefotaxime should be administered in patients with *S. pneumoniae* meningitis before antibiotic susceptibility results are available(1, 3). The length of antimicrobial therapy courses is not fixed; an analysis of randomized controlled trials has evaluated the efficacy and safety of short-course antibiotic therapy for bacterial meningitis (6). This study has used long and short courses of therapy which has involved children (aged 3 week to 16 year) . No difference was demonstrated in the end of therapy in relation to clinical success, long-term neurological complications, long-term hearing impairment, total adverse events, and secondary nosocomial infections between short-course (4-7 days) and long-course (7-14 days) treatment with intravenous ceftriaxone. The American Academy of Pediatrics does not endorse a shorter course of therapy than 5-7 days for meningococcus, 10 days for *H influenzae,* and 14 days for *S pneumonia* (6). Although the available evidence is limited, some studies show no difference between short-course and long-course antibiotics for bacterial meningitis in children (7).

According our experience we found antibiotic treatment of purulent meningitis caused by *Hib*, *N. meningitides*, or *S. pneumoniae* can be safely discontinued in children who are stable by day five. However, this approach should not be considered the standard of care in all meningitis cases (8). Our guidlines in the Fever hospital in Baghdad for treatment of community-acquired meningitis is seven days for *N. meningitides*, ten days for *Hib* and no less than two weeks hospital treatment for *S. pneumoniae*. For hospital- acquired meningitis cases, the treatment is continued for three weeks. We treated our patients during the critical time of blockade on Iraq after the dessert storm in 1991, with great shortage in the antibiotics and other medical supplies for Iraq and therefore the choice of the best antimicrobial coverage was lacking.

Conclusions

The empirical treatment for bacterial meningitis is still the rule before bacterial isolation and susceptibility tests is available. Different antibiotics carefully chosen and given singly or in combination can offer optimum results. The length of treatment is still controversial, however, shorter courses can be enough for cure and being cost benefit effective. Nosocomial meningitis needs careful awareness and choice of antibiotics to cover the hospital acquired resistance pathogens for longer periods than the community-acquired meningitis.

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