Postgrad Med J 1995; 71: 36–38 © The Fellowship of Postgraduate Medicine, 1995

Bacterial meningitis in the first three months of life

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Summary

A retrospective study of infants with bacterial meningitis admitted to our hospital during 1949–52, highlighted the lack of 'classical' signs of meningitis in these infants.[1] We carried out a similar review of 44 infants aged less than three months, admitted during 1982–91. We also determined the causative organisms and their antiobiotic sensitivities.

Symptoms and signs were similar in the two series. Forty infants in the later series were either febrile, irritable or had seizures on the day of admission. Overall mortality fell from 30% to 11%.

Between 1982 and 1991 Group B *Streptococcoccus* and *Neisseria meningitidis* were the commonest causes of meningitis. All organisms, except one, were sensitive to ampicillin and/or cefotaxime.

Bacterial meningitis should be suspected in young infants who are febrile, irritable or having seizures. Initial treatment with ampicillin and cefotaxime is appropriate.

Keywords: bacterial meningitis, infants

Introduction

Bacterial meningitis in the first few months of life presents a number of difficult clinical problems in diagnosis and treatment. The symptoms and signs of meningitis may be non-specific, and diagnosis relies heavily on a high index of suspicion.

Forty years ago Haworth[1] noted that the 'classical' signs of meningitis (neck stiffness and/or a raised anterior fontanelle) occurred less often in infants less than three months of age. He reported on 13 infants under three months of age with bacterial meningitis admitted to our hospital between July 1949 and April 1952. The diagnosis of meningitis was delayed in four infants, all of whom died. Since this study, group B *Streptococcus* has become a major pathogen for young infants.[2] We aim to see if the clinical presentation of bacterial meningitis in young infants has changed since Haworth's study. We also aim to determine whether delay in diagnosis still occurs.

Controversy also exists over the most appropriate initial antibiotic regimen for young infants with meningitis. The organisms that cause bacterial meningitis in infants vary with the age of the child. In the neonatal period Gram-negative bacteria (particularly *Escherichia coli*), and more recently Group B *Streptococcus* (GBS), and *Listeria monocytogenes*, are common causes.

In children over three months of age *Neisseria meningitidis*, *Haemophilus influenzae* type b (Hib) and *Streptococcus pneumoniae* cause almost all community-acquired cases.[3] Infants between one and three months of age can develop meningitis with either the neonatal or the childhood group of pathogens. Antibiotic guidelines based on knowledge of the common pathogens recommend a combination of cefotaxime and ampillicin.[4] Before adoption, these guidelines need validating in a clinical setting.

Neonatal meningitis has a high mortality, especially in premature and low birth weight infants.[3] Initial treatment with penicillin, cefotaxime and gentamicin is recommended.[5]

Almost half of all cases of neonatal meningitis are admitted to hospital directly from home[3] and will therefore not be treated on a neonatal unit but on a paediatric ward. An antibiotic regimen to cover meningitis in all children under three months of age admitted to paediatric wards may help to simplify treatment.

We have reviewed infants under three months of age with bacterial meningitis admitted to our hospital over a 10-year period. Our aim was to examine the initial clinical presentation and to determine the causative organisms and their antibiotic sensitivities. An appropriate initial antibiotic regimen could then be suggested.

Patients and methods

The case-notes of all children less than three months of age with positive cerebrospinal fluid (CSF), cultures, admitted to our hospital between January 1982 and December 1991, were reviewed. Cases were identified from microbiology records and ward admission books. The case-notes for all but three children were eventually traced, and information from previous research was available on two of these children. Infections complicating myelomeningocoeles, ventricular shunts, or occurring after surgery were excluded.

Forty-five episodes of meningitis occured in 44 children over the 10-year period. (One child was re-admitted following partially treated *E coli* meningitis.) Six infants had been born

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Accepted 27 July 1994

before 37 weeks of gestation, but all been discharged from a neonatal unit before their admission with meningitis.

Twenty-nine infants were directly admitted to our hospital, one of whom was re-admitted, and 15 were tertiary referrals.

Five children died, three of whom had neonatal meningitis (see table 1).

Results

SYMPTOMS AND SIGNS

Presenting symptoms and signs were noted from case-notes, referral letters and casualty cards and compared with those found by Haworth[1] (table 2).

Symptoms and signs did not differ between the two groups except for the incidence of poor feeding. Forty children in our series presented with either fever, irritability or seizures on the day of admission. Two further infants had poor peripheral perfusion and cyanosis. The 'classical' signs of meningitis (neck stiffness and/or a raised anterior fontanelle) were absent in over 50% of infants in both series. A clinical diagnosis of meningitis was made in only 43% of these infants in Haworth's series, but in 81% of these infants in our series. Delay in diagnosis occurred in four children in Haworth's series. These infants were initially thought to have pneumonia (two), jaundice, or failure to thrive. All these children died. In our series delay in diagnosis occurred in seven cases. Five children were initially referred to other specialities because of presumed surgical (three) or cardiac (two) symptoms, one child presented with afebrile seizures, and one with stomatitis. None of these children died. There was an overall decrease in mortality from 30% to 11%, but this failed to achieve statistical significance.

Table 1 Causative organism of meningitis in infants under three months, Alder Hey Children's Hospital 1982–91. Figures are given as the number of admissions with the number of deaths in parentheses

	Age in completed week			
Organism	*0–3*	*4–8*	*9–13*	*Total*
N meningitidis		8	5	13
H influenzae		1	1(1)	2
S pneumoniae	1	2(1)	1	4
Group B Strep	8(2)	4	3	15
Group A Strep	3(1)			3
Listeria	2			2
Escherichia coli	2	2*		4*
Other**	1		1	2

*One child with relapsed *E coli* meningitis re-admitted aged five weeks.
***Streptococcus milleri* (one week old) and *Enterobacter agglomerans* (10 weeks old).

Table 2 Presenting symptoms and signs and outcome of infants less than three months with bacterial meningitis

	1949–52	*1982–91*
Symptoms	(n = 13)	(n = 42)
Poor feeding	5 (38%)	32 (76%)*
Fever	NA	29 (69%)
Irritable	7 (54%)	25 (60%)
Lethargic	1 (8%)	14 (33%)
Vomiting	5 (38%)	13 (31%)
Signs	(n = 13)	(n = 40)
Temperature ⩾ 38°C	NA	28 (70%)
Irritable	NA	28 (70%)
Seizures day 1	NA	14 (35%)
Full fontanelle	5 (38%)	18 (45%)
Neck stiffness	3 (23%)	5 (13%)
No 'classical' signs	7 (56%)	22 (55%)
Outcome	(n = 13)	(n = 45)
Delay in diagnosis	4 (30%)	7 (15%)
Deaths	4 (30%)	5 (11%)

NA = information not available
*Significant at $p < 0.05$ by chi^2.

ORGANISMS

The organisms grown from the CSF of the children admitted between 1982 and 1991 are listed in table 1. Ten infants aged between one and three months (36%) had infections with 'neonatal' organisms. Both cases of coliform meningitis in this age group were due to a relapse of infection. (One child had previously been treated at our hospital and one at a referring hospital.)

Antimicrobial sensitivities were available for 41 organisms, 28 of which were seen on microscopy of the CSF. Of the 17 organisms isolated from neonates, 11 were sensitive to either penicillin or cefotaxime and four organisms (*E coli* and *L monocytogenes*, two each) were sensitive to gentamicin. (Sensitivities were unavailable for two cases of GBS meningitis.) However all 15 organisms with known sensitivities were sensitive to either ampicillin or cefotaxime, making the addition of gentamicin unnecessary.

Amongst the 26 organisms with known sensitivies in the one to three month age group, all except one were sensitive to either ampicillin or cefotaxime or both. The exception was a case of relapsed meningitis due to *E coli* resistant to ampicillin. This organism was sensitive to cefuroxime, but sensitivity to cefotaxime was not tested. (This case occurred in 1982.) (Sensitivities were again unavailable for two cases of GBS meningitis.)

Discussion

Symptoms and signs of bacterial meningitis in young infants appear not to have changed over the past 40 years despite changes in the causative organisms.[2] (There were no cases of GBS meningitis in Haworth's series.) A high index of suspicion is still necessary as over half the cases do not show the 'classical' signs of bacterial meningitis. Most cases in our series, however, were either febrile, irritable or had seizures on the day of admission. Other studies have found that fever and irritability are the commonest signs of bacterial meningitis in young infants.[6,7] Awareness of these non-specific symptoms of meningitis appears to be increasing, as a delay in diagnosis occurred in a much smaller proportion of cases in our series (31% in Haworth's series, 16% in ours). There

is no room for complacency, however, as the five infants initially referred to our surgical and cardiac colleagues demonstrate.

Our study demonstrates the wide number of pathogens causing meningitis in the first three months of life, with GBS and meningococci predominating. All except one of these organisms were sensitive to either ampicillin or cefotaxime, or both. (The exception being a relapsed case of menigitis due to *E coli* sensitive to cefuroxime, and thus likely to be sensitive to cefotaxime, although not tested.) The four cases where sensitivities were unavailable were all caused by GBS. These would almost certainly be sensitive to ampicillin and cefotaxime.

Studies from the US found that Hib[8] or GBS[6] were the commonest causes of meningitis in infants aged between one and three months, and recommended treatment with ampicillin combined with either chloramphenicol[8] or cefotaxime.[6] No similar study from the UK, focusing on this age group, has been published although de Louvois *et al* have studied meningitis in children under one year of age.[3] In this study, 10% of neonatal meningitis was caused by the common childhood organisms, and 5% of meningitis between the second and sixth month of life was caused by neonatal organisms.

Penicillin and chloramphenicol were the most commonly used antibiotics for both neonates and older infants. Chloramphenicol and gentamicin both have serious side-effects and require monitoring of blood levels.[9] The efficacy and safety of ampicillin and cefotaxime make them an attractive choice for young infants with bacterial meningitis.[4] This combination is increasingly popular amongst directors of programmes in paediatric infectious disease in the US.[10] Our study shows that this combination could be used in the UK as the initial treatment of meningitis in infants aged between one and three months. Neonates admitted to a children's ward with meningitis could also be treated with this regimen, instead of one using gentamicin combined with cefotaxime and penicillin.[5]

Bacterial meningitis in infants

- classical signs often lacking
- group B *Streptococcus* and *N meningitidis* are the usual causes
- high index of suspicion for diagnosis
- treat initially with ampicillin and cefotaxime

Our study cannot make any recommendations about treating meningitis on the neonatal unit, although a combination of ampicillin and cefotaxime has been recommended by others.[11,12]

In conclusion, the diagnosis of bacterial meningitis in young infants continues to require a high index of suspicion. Meningitis should be suspected in any infant less than three months of age who is febrile, irritable, has seizures or is in a poor condition. Initial treatment on a paediatric ward with ampicillin and cefotaxime is appropriate until the causative organism is identified.

We would like to thank Dr Omnia Marzouk and Dr Huw Thomas for providing data, Paula Thomas for help in tracing case-notes, and the Johanne Holly Trust for financial support.

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