

CHANGING PATTERN OF ANTIBIOTIC SENSITIVITY OF NEISSERIAE MENINGITIDIS FROM CHILDREN WITH MENINGOCOCCAL MENINGITIS IN NORTH EASTERN NIGERIA

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ABSTRACT

Objective: To determine the changing pattern of antibiotic sensitivity of *Neisseriae meningitidis* from children with Meningococcal meningitis in North Eastern Nigeria.

Materials and Methods: This study was carried out over 31 months, from January 2003 to July 2005 in the Paediatric ward of Federal Medical Centre (FMC), Azare. The cerebrospinal fluid (CSF) of all patients with clinical features of meningitis admitted were examined microbiologically, including culture for bacterial organisms and their sensitivity pattern as well as biochemical tests determined.

Results: The CSF specimens from 44 patients, aged between 2 months and 12 years (20 females and 24 males) yielded gram negative intracellular diplococci by gram staining. Of these, *Neisseriae meningitidis* was cultured in 18 (40.9%). The remaining bacterial isolates did not survive culture. The analysis of antibiotic sensitivity of *Neisseriae meningitidis* from the eighteen CSF specimens showed 100 per cent sensitivity to ceftriaxone. Resistance of the bacterial isolates to benzyl penicillin, ampicillin and chloramphenicol was 80 %, 71.4% and 20% respectively. Varying levels of sensitivity of the organisms to augmentin (amoxicillin-clavulanic acid), gentamicin and cotrimoxazole were also documented.

Conclusion: This study highlights the increasing resistance of *Neisseriae meningitidis* to empirically used antimicrobial drugs.

Key Words: Antibiotics Sensitivity, *Neisseriae Meningitidis*, Children, Northeastern Nigeria. (Accepted 7 March 2008)

INTRODUCTION

Epidemics of meningococcal meningitis occur towards the end of the dry season when it is hot, dry and dusty and stop shortly after the onset of the rains.¹⁻³

Azare, the headquarter of Katagum Local Government Area of Bauchi State, North Eastern Nigeria with a population of 95,423 is situated on latitude 11.55° NE and Longitude 10.10° east of the Sudan Savannah. It falls within the meningitic belt of Africa, experiencing epidemics since 1840.⁴

Antibiotic treatment is usually started empirically with benzyl penicillin and chloramphenicol while awaiting results of microscopy, culture and sensitivity. Delay and inappropriate initial treatment of meningococcal infection is often accompanied by poor outcome.⁵

In this study, we report the changing pattern of antibiotic sensitivity of *Neisseriae meningitidis*.

PATIENTS AND METHODS

The Cerebrospinal fluid of all patients with clinical features of meningitis admitted into the Paediatric ward of FMC, Azare from January 2003 to July 2005 (31 months) were analysed and the pattern of antibiotic response of meningococcus recorded. Demographic data including age, sex, and place of residence were recorded as well as vaccination status against meningococcal meningitis. The symptoms and signs were documented and the clinical progress of the patients closely monitored.

Lumbar puncture (LP) was done in all patients with clinical features suggestive of meningitis who were clinically stable. The CSF was analysed by gram staining and cultured on Blood agar and Chocolate agar plates and sensitivity pattern determined.

The diagnosis of Meningococcal meningitis was based on CSF culture results in addition to CSF cellular and chemical changes. CSF samples were also analysed for protein and glucose with simultaneous CSF/ blood glucose ratio, total and differential white cell count.

The bacterial isolates that survived culture were tested against microbial drugs including benzyl penicillin, ampicillin, chloramphenicol by standard disc diffusion method⁶ using oxoid sensitivity disc and other discs for ceftriaxone, augmentin (amoxicillin-clavulanic acid), gentamicin and cotrimoxazole. The sensitivity pattern was read as sensitive or resistant using zone of inhibition comparable to the standard sensitive organism. Blood culture was not done because of unavailability of culture media. Other laboratory investigations were carried out as dictated by the clinical state of the patient.

Patients' treatment was commenced with combination of chloramphenicol and benzyl penicillin or ceftriaxone alone empirically on admission to cover the three commonest causative organisms; *Neisseriae meningitidis*, *Haemophilus influenzae* type b and *Streptococcus pneumoniae* as their clinical presentations may be indistinguishable^{7,8} pending the sensitivity results. Statistical analysis was by chi-square method; p-values < 0.05 were considered significant.

RESULTS

Over the study period, CSF specimens of 44 patients, aged between 2 months and 12 years from 20 females and 24 males (1:1.2) yielded gram negative intracellular diplococci by gram staining. Of these, *Neisseriae meningitidis* was cultured in 18 (40.9%). The remaining bacterial isolates did not survive culture. Thirteen out of the 18 bacterial isolates were tested for sensitivity while 5 were not. All the 13 bacterial isolates were sensitive to ceftriaxone (100%). The sensitivity of the 15, 14 and 15 out of the 18 bacterial isolates to chloramphenicol, ampicillin and benzyl penicillin was 80%, 28.6% and 20%, respectively (Table 1). The difference between sensitivity of bacterial isolates to ceftriaxone with chloramphenicol was not statistically significant (p=0.23), while, the difference between the sensitivity of the isolates to ceftriaxone with benzyl penicillin, ceftriaxone with chloramphenicol and benzyl penicillin combination and ceftriaxone with ampicillin was statistically significant (p=0.00). The *Neisseriae meningitidis* isolates also showed sensitivity of 40% each to augmentin (amoxicillin-clavulanic acid) and gentamicin, while that of ampicillin and cotrimoxazole was 28.6% and 23.1%, respectively. Antibiotic discs were not always available; therefore, sensitivity results were not available for all *Neisseriae meningitidis* isolated.

Some of the children also presented with other forms of meningococcal infection such as limb and digital gangrene and arthritis. The overall mortality rate was 11.4%.

Table 1: **Antibiogram of *Neisseriae Meningitidis* Isolates from CSF.**

Antibiotics	S (%)	R (%)	NT
Ceftriaxone	13 (100%)	0 (0%)	5
Chloramphenicol	12 (80%)	3 (20%)	3
Augmentin (amoxicillin-clavulanic acid)	6 (40%)	9 (60%)	3
Gentamicin	6 (40%)	9 (60%)	3
Ampicillin	4 (28.6%)	10 (71.4%)	4
Cotrimoxazole	3 (23.1%)	10 (76.9%)	5
Benzyl penicillin	3 (20%)	12 (80%)	3

S = Sensitivity, R = Resistance and NT = Not tested.

Ceftriaxone with Chloramphenicol
Fisher exact: 2 tailed, p-value = 0.23

Ceftriaxone with Benzyl penicillin
 $X^2 = 18.20$, p-value = 0.0000199

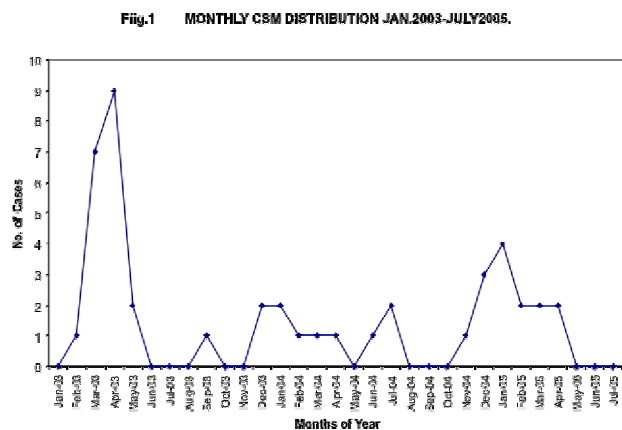
Ceftriaxone with Chloramphenicol and Benzyl penicillin combination

$X^2 = 21.87$, p-value = 0.0000178

Ceftriaxone with Ampicillin

Fisher exact: 2 tailed, p-value = 0.0001526

Figure 1: **Monthly Distribution of Cases from Jan 2003 to July 2005.**



DISCUSSION

In over five decades since epidemic of meningococcal meningitis was described in Northern Nigeria, the African meningitic belt has not changed.⁴ The periodicity of meningococcal meningitis epidemics of 5-10 years has been replaced by annual epidemics in the West African region of the meningitic belt.⁹ The occurrence of epidemics of meningococcal meningitis during the hot dry season with high ambient temperature and low humidity experienced just prior to the onset of the rainy season has been established,¹⁻³ as reported in our study. In addition to the meningococcal meningitis, other forms of meningococcal infection were reported in some of the children.¹⁰ In this study, the overall

mortality was 11.4% which is similar to that of a previous report.¹¹

The treatment of meningococcal meningitis has evolved over time from the use of sulphonamides, long-acting oily chloramphenicol, and penicillin alone or in combination with chloramphenicol to cephalosporins.

With reports of emergence of resistant strains of meningococcal organisms to chloramphenicol¹² and penicillins,^{13,14,15} the infection poses a great threat to effective antibiotic therapy in resource-poor countries of the meningitis belt where cephalosporins as alternative antibiotics are not readily available and affordable.

This study further buttresses the increasing resistance of *Neisseriae meningitidis* to benzyl penicillin (80%), ampicillin (71.4%) and to some extent, chloramphenicol (20%).

Limitation of medical facilities precludes laboratory investigations such as rapid immunological tests and blood culture in this centre, like most health centres in the meningitic belt.

Control measures such as regular surveillance, prevention of overcrowding by improving socioeconomic status, health education and mass vaccination are recommended as in previous studies.^{10,16-19}

In conclusion, this study highlights the changing pattern of antibiotic sensitivity of *Neisseriae meningitidis* and resistance of the organism to the empirically used antibiotics such as penicillin, ampicillin and to a lesser extent chloramphenicol.

Though our sample size was small, in view of the increasing resistance of *Neisseriae meningitidis* to benzyl penicillin, ampicillin and even chloramphenicol, and 100 per cent sensitivity to ceftriaxone, it is suggested that larger and multicentred studies be conducted to determine the current antibiotic sensitivity of *Neisseriae meningitidis* to validate this findings. The use of ceftriaxone as first line drug in the treatment of meningococcal infection as suggested by Akpede²⁰ is hereby advocated and in its absence, chloramphenicol still remains a single drug to be used as initial treatment in the management of meningococcal meningitis.

The provision of rapid immunologic diagnostic kits and blood culture media for routine laboratory use is also recommended.

ACKNOWLEDGMENT

The authors are grateful to the nursing and medical records personnel of FMC Azare for their assistance. We thank the management of the Hospital for granting approval for the study. The helpful suggestions by colleagues are equally acknowledged.

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