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OUTCOME OF PNEUMOCOCCAL MENNINGITIS IN CHILDREN TREATED WITH AMPICILLIN-CHLORAMPHENICOL AND A THIRD-GENERATION CEPHALOSPORIN

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ABSTRACT

This study done to compare the outcome of patients with pneumococcal meningitis treated with Ampicillin-Chloramphenicol with those treated with a third-generation cephalosporin. Mortality rate and development of sequelae were likewise compared between treatment groups. Profile of patients with pneumococcal meningitis were described. Patients diagnosed with pneumococcal meningitis on CSF culture and treated with Ampicillicin-Chloramphenicol for 10-14 days or Cefoxtamine/Ceftriaxone at Philippine Children's Medical Center between August 2003 were included in the study. Patients treated with Ampicillin-Chloramphenicol were separated from those treated with Cefotaxime or Ceftriaxone, and the two groups were compared in terms of morality rate and development of sequelae. In this study, the disease occurred predominantly in children less than one year old. No sex predilection was observed. The most common presenting sign was seizures which was the primary reason for consultation. Other manifestations included cough and colds, increased tone, irritability, bulging anterior fontanelle, and nuchal rigidity. The most common predisposing factor in the development of *Pneummococcal* meningitis was pneumonia. Outcome was not significantly different among the treatment groups although the duration of hospital stay was significant different among the three groups. The most common neurologic sequelae in patients with *Pneumococcal* meningitis was the development of hydrocephalus followed by seizures.

INTRODUCTION

Bacterial meningitis is one of the most potentially serious infections in infants and older children. It is associated with a high rate of acute complications and risk of chronic morbidity. The etiology is age dependent, and risk factors for meningitis vary. The usual clinical course is preceded by an upper respiratory tract or gastrointestinal symptoms followed by signs of central nervous system infection. The less common presentation is that in which shock, disseminated intravascular coagulopathy, reduced level of consciousness, and death occur[1].

Keywords: *outcome, pneumococcal meningitis*
* *Philippine Children's Medical Center*
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SIGNIFICANCE OF THE STUDY

Before the discovery and use of antibiotics, bacterial meningitis generally was fatal. Although antibiotic therapy has improved the prognosis in patients afflicted with bacterial meningitis dramatically, it continues to be a significant cause of morbidity and mortality in children[2].

In the United States, the Center for Disease Control and Prevention estimated in 1972 29,000 cases of meningitis caused by *H. influenzae type b*, 4800 cases cases caused by *S. pneumoniae*, and 4600 cases caused by *N. meningitides*. Since meningococcal meningitis has the most reported, followed by *S.pneumoniae*, and *H. influenzae*. Group B *Streptococcus* has been noted as the most common cause of meningitis in children 2 to 6 weeks of age followed by *E. coli, L. monocytogenes, H. influenzae,* and *S. pneumoniae*[3].

With the virtual elimination of *H. influenzae* meningitis, *S. pneumoniae* has become the most common cause of bacterial meningitis among children of all age groups beyond the neonatal period[4].

In term of morality rates, Davey and associates reported that between 1968 to 1977, *N. meningitidis* accounted for 3.5% of deaths, *H. influenzae* accounted for 7.7% and *S. pneumoniae* accounted for 30%[5].

For many years, Ampicillin and Chloramphenicol were preferred as the initial empiric therapy for children older than 3 months of age and suspected of having bacterial meningitis. The development of newer cephalosporins and other antibiotics that have excellent bactericidal activity within the CSF has led to several possible alternative approaches to the initial therapy of meningitis. Experience with Cefotaxime and Ceftriaxone continues and these drugs have become the treatment of choice in most centers with the development of Penicillin resistant strains. A survey of directors of programs in the United States of Pediatric infectious diseases in 1992[6] indicated that 92% used Cefotaxime or Ceftriaxone, compared with 2 percent who continued to use Ampicillin and Chloramphenicol. This is a dramatic change from a 1988 survey in which Ampicillin

and Chloramphenicol still were found to be used most frequently for initial empiric therapy[7].

The incidence of systemic infection with penicillin-resistant *Steptococcus pneumoniae* was increased steadily worldwide since first reported in Australia in the 1960s and was became an increasing problem in the USA since the mid 1980s[8]. A nationwide survey documented that 6.6% of isolates were resistant to penicillin (minimal inhibitory concentration >0.1 ug/ml). Resistance to Cefotaxime and Ceftriaxone also was evident in 5-10% of isolates.

The first report of meningitis caused by resistant pneumococci was published in 1974, and numerous case reports have appeared subsequently[9]. More recently, there was an increased in the number of cases of systemic infection and meningitis caused by *S. pneumoniae* resistant to Penicillin and third-generation cephalosporins.

The purpose of this study was to described the outcome of patients with *Pneumococcal* meningitis treated with Ampicillin an Chloramphenicol and with those treated with a third-generation cephalosporin in terms of mortality and survival rate, and in the subset of survivors, the development of sequelae. The increasing frequency of *S. pnuemoniae* resistant to B-lactam drugs may necessitate a change in empirical therapy in the treatment of Pneumococcal meningitis and thus improve survival rate and long-term outcome of these patients.

OBJECTIVES

General Objectives

To describe the outcome of patients with Pneumococcal meningitis treated with Ampicillin and Chloramphenicol and those treated with a third-generation cephalosporin.

Specific Objectives

1. To describe the outcome of patients with Pneumococcal meningitis treated with Ampicillin and Chloramphenicol and those treated with a third-generation cephalosporin in terms of the following:
   a. mortality rate
   b. development of sequelae (hearing loss, language disorders or delayed language development, inability to read, impaired vision, mental retardation, motor abnormalities, hemiparesis, spasticity, seizures, and hydrocephalus)
2. To describe the profile with Pneumococcal meningitis in terms of the following:
   a. age distribution
   b. sex predilection
   c. predisposing factors (otitis media, pneumonia, sepsis, malnutrition)
   d. clinical manifestations
   e. cerebrospinal fluid (csf)
   f. neurosonographic findings

METHODOLOGY:

Study design

Retrospective study

Patient Eligibility

INCLUSION CRITERIA

Patients diagnosed with Pneumococcal meningitis on cerebrospinal fluid culture who were seen treated with Ampicillin at 200 mg/kg/24 hr and Chloramphenicol at 100 mg/kg/24 hr for 10-14 days or a third-generation cephalosporin (Cefotaxime 200mg/kg/ 24 hr or Ceftriaxone 100 mg/kg/24 hr for 10-14 days) at Philippine Children's Medical Center between August 1989-August 2003 were included in the study.

EXCLUSION CRITERIA

Patients who developed Pneumococcal meningitis with concomitant congenital or acquired abnormalities of the immune system, congenital asplenia or post-splenectomy states, sickle-cell disease, and systemic disease (such as diabetes mellitus, renal and adrenal insufficiency,cystic fibrosis, and hypothyroidism) were excluded. Likewise, those with congenital or acquired CSF leak across a mucocutaneous barrier and those with incomplete data were exclude from the study.

DESCRIPTION OF STUDY PROCEDURES

Patients who fulfilled the set criteria were included in the study.

Laboratory logbooks were checked and cases of culture positive Pneumococcal meningitis between August 1989 to August 2003 were identified. Important patient data (name, age,sex,date of csf culture) were obtained to facilitate retrieval of charts from the medical records section. The profile of such patients were studied and the following were abtained: age and sex, address, period of hospital stay. Admission and final diagnosis, predisposing factors for meningitis (otitis media, penuemonia, sepsis, malnutrition) clinical manifestations, CSF finding, and neurosonographic findings. Patients treated with Ampicillin and

Choramphenicol were separated from those treated with Cefotaxime or Ceftriaxone, and mortality rate and development of sequelae were noted between the two groups. Patients treated initially with Ampicillin and Chloramphenicol then shifted to a third-generation cephalosporin were identified and the reason for such were noted.

As for the development of sequelae, those who developed hearing loss, language disorder or delayed language development, inability to read, impaired vision, mental retardation, motor abnormalities, hemiparesis, spasticity, seizures, and hydrocephalus as a consequence of Pneumococcal meningitis were identified by review of charts on follow-up.

STATISTICAL ANALYSIS

Frequency distribution, mean, standard deviation, and percentages were used for descriptive data.

Analysis of variance, chi-square, and post-hoc t-test were used whenever appropriate.

RESULTS

Seventy two patients were identified to have Pneumococcal meningitis on cerebrospinal fluid culture. Of these, only fifty eight (80 %) records were retrieved for review. Thirty four (58.62 %) patients were eligible for the study. Of these, twenty three charts (67.65%) were retrieved on follow-up.

Table 1 shows the socio-demographic profile of patients with Pneumococcal meningitis. It can be seen that there is an equal number of male and female patients. There was a higher proportion of females in the 0-1 year age group, but there was a higher proportion of males in the older age groups. Most of the subjects were service patients.

Table 1. Sociodemographic profile of patients with pneumococcal meningitis, 1989-2003

	N		%	
	M	F	M	F
Age in years				
0-1	13	16	76.5	94.1
>1-4	3	1	17.6	5.9
>4-10	1	0	5.9	0
Socio-economic Status	**N**		**%**	
Pay	1		2.9	
Service	28		82.3	
Pay to Service	5		14.7	

Table 2 shows that the most common admitting impression was bacterial meningitis, (88.3%) followed by seizure disorder, viral encephalitis, and bacterial meningitis with empyema. The most common presenting signs and symptoms were seizures (82.3%), followed by cough/colds, bulging frontanelle, hyperreflexia, and irritability, in that order.

Table 2. Admitting diagnosis and signs and symptoms of pneumococcal meningitis, 1989-2003

	N=34	%
Admitting Diagnosis		
Bacterial Meningitis	30	88.3
Seizure	2	5.9
Viral encephalitis	1	2.9
Bacterial Meningitis with Empyma	1	2.9
Signs and symptoms		
Anorexia	5	14.7
Vomiting	6	17.6
Cough/colds	20	58.8
Irritability	15	44.1
Seizures	28	82.3
Bulging fontanelle	18	52.9
Nuchal rigidity/Meningeal irritation	18	52.9
Hyperreflexia	18	52.9
Papilledema	1	2.9
Focal deficits	3	8.8
Altered consciousness	14	41.2

Table 3. shows that the most common predisposing factor was pneumonia (35.3%), followed by URTI (29.4%), malnutrition (26.4%), sepsis due to *Streptococcus pneumoniae* (23.5%) and clinical sepsis (11.8%).

Table 3. Predisposing factors among patients with pneumococcal meningitis, 1989-2003

	N	%
URTI	10	29.4
Otitis Media	0	0
Pneumonia	12	35.3
Sepsis SP	8	23.5
Malnutrition	9	26.4
Sepsis, clinical	4	11.8

Table 4 shows that meningitis was the most common finding on ultrasound, followed by hydrocephalus, and lastly empyema. Other findings include cerebral edema and subdural effusion. A small percentage had normal findings.

The table also shows that more than two thirds of the subjects had WBC counts of less than or equal to 250 in the CSF; 14.7% had counts ranging from 251-350 while 2.9% had up to 450 WBCs in the CSF. About one third of the subjects had lymphocyte counts from 61-80 while, one fourth had counts from 21-40. One third had a polymorphonuclear count from 21-40. More than half of the subjects had protein levels of <3. More than half had sugar levels between 1-10%.

Table 4. Result of Cranial Ultrasound and CSF examination of Pneumococcal Meningitis, 1989-2003

	N	%
Cranial Ultrasound		
Meningitis	22	64.7
Hydrocephalus	20	58.8
edema	4	11.8
empyema	6	17.6
effusion	4	11.8
Normal	3	8.8
CSF Findings		
WBC		
<=250	22	64.7
251-350	5	14.7
351-450	1	2.9
451-550	0	0
451-650	2	5.9
651-750	0	0
751-850	2	5.9
850+	2	5.9
Lymphos		
<=20	4	11.8
21-40	9	26.5
41-60	7	20.6
61-80	11	32.3
81-100	3	8.8
100+	0	0
Polys		
<=20	5	14.7
21-40	11	32.3
41-60	8	23.5
61-80	6	17.6
81-100	4	11.9
100+	0	0
Protein		
<3	18	52.8
>3	15	44.0
Sugar (%)		
<1	1	2.9
1-10	19	55.9
11-20	4	11.7
21-30	4	11.7
31-40	2	5.9
41-50	4	11.7
50+	8	23.5

Table 5 shows that Ampicillin/chloramphenicol was given to 44.1% of the subjects in the study group, 41.1% were shifted from ampicillin-chloramphenicol combination to ceftriaxone or cefotaxime, and 5 or 14.8% were treated from the start with ceftriaxone or cefotaxime. The most common reasons for shifting from ampicillin-chloramphenicol combination to a third-generation cephalosporin was unchanged CSF findings, and worsening of clinical condition warranting intubation. The mean duration of treatment before a shift in antibiotic was 3 days.

Table 5. Treatment of Pneumococcal Meningitis, 1989-2003

	N	%
Treatment		
Ampicillin/Chloramphenicol	15	44.1
Ceftriaxone/Cefotaxime	5	14.8
Shifted from Ampicillin/ Chloramphenicol to Cephalosporin	14	41.1
Reason for shifting		
No change in CSF	6	42.9
Intubated	6	42.9
Hydrocephalus	1	7.1
Seizure	1	7.1

Outcome was not significantly different in the three treatment groups. Majority or 80% were discharged improved, and a final diagnosis of bacterial meningitis was the most common diagnosis for the three groups. Length of treatment was significantly different

Table 6. Outcome, Final Diagnosis, Length of Treatment of Pneumococcal Meningitis, 1998-2003

	Group 1 Ampicillin/ Choram-phenicol	Group 2 Ceftriaxone Cefotaxime	Group 3 Shifted from group 1 to 2	P value
	(n=15)	(n=5)	(n=14)	
Outcome				
Alive, improved	12 (80%)	4 (80%)	11 (79%)	0.994
Died	2 (13.3%)	1 (20%)	2 (14.3%)	0.934
Home against advice	1	0	1	0.299
Final diagnosis				
Bacterial Meningitis	14	4	10	0.299
Bacterial Meningitis with Empyema	1	1	4	
Length of treatment				0.023
X	13.13	19.0	26.36	Significant
SD	6.33	11.49	16.38	pair: Group 1 and 3

among the three groups, with length of treatment in the ampicillin-chloramphenicol group significantly shorter than those shifted from ampicillin-chloramphenicol to a third-generation cephalosporin. All variables for sequelae were not significantly different among the three groups as shown in Table 7.

Table 7. Sequelae of Pneumococcal Meningitis, 1989-2003

Sequelae	Group 1	Group 2	Group 3	
Hydrocephalus	5	1	7	0.432
Seizure	4	1	1	0.382
Spasticity	7	1	8	0.360
CN palsy	1	0	0	0.496

DISCUSSION

Those factors that predispose the host to infection in other sites also predispose the host to bacterial infection of the central nervous system. There was a strong interrelationship of factor relating to the host, organism, and environment with regard to the pathogenesis and outcome of meningitis[2].

An increased incidence of bacterial meningitis is observed in the very young[2]. In this study, twenty nine of the thirty four patients (85.3%) studied were one year old or younger.

The increased incidence of septicemia and meningitis in this age group was reflective of physiologic deficiencies or immaturity of host defense mechanisms. These include decreased phagocytes and bactericidal activity of leukocytes, defects in the response of leukocytes to chemotactic factor, and a deficiency in the capacity to support opsonization, These infants likewise have deficiencies in serum complement and serum immunoglobulins (IgM and Iga).

Males were affected more frequently than females, and the severity of disease also was increased in these groups[10]. However, the above finding was not noted in this study where an equal number of male and female patients were seen.

Additional risks to develop meningitis include recent colonization with pathogenic bacteria, close contact with individuals having invasive disease, crowding, and poverty[1]. In this study, twenty eight of the thirty four patients (82.35%) belonged to families of low socio-economic status.

Bacterial colonization of the nasopharynx with a potentially pathogenic microorganism was the usual source of bacteremia which usually precedes meningitis. There may be prolonged carriage of the colonizing organisms without disease or, rapid invasion after recent colonization. Prior or concurrent viral upper respiratory tract infection may enhance the pathogenicity of bacteria producing meningitis. In this study, the mean duration from the onset of symptoms to the full blown picture of pneumococcal meningitis was four days. Upper respiratory tract infection was noted in ten (29.4%) of the thirty four patients, and pneumonia was noted in twelve. (35.3%)

Bacterial meningitis follows a period of bacteremia and it had been show that in patients with pneumococcal meningitis, 52% of children had positive blood cultures[11]. Of these, 44% of the entire group had received some form of antibiotic therapy before admission to hospital and before these blood cultures were obtained. If these individuals were excluded positive blood cultures would be expected in about 80% of patients. In this study, of the 34 patients studied, eight (23.53%) had a positive blood culture. Four of the thirty four patients (11.76%) exhibited signs of sepsis but were culture negative. Majority had no previous antibiotic intake (82.5%).

Bacteria meningitis in children with otitis, media generally follows bacteremia, although direct invasion of the meninges may occur as a complication of otitis media[2]. In this study, none of the thirty four patients had otitis media as a predisposing factor in the development of meningitis.

Malnutrition also predisposes children and adults to infectious diseases due to impaired cellular immune response and impaired phagocytosis which have been documented in malnourished children[12]. In this study, only nine of the thirty four patients studied (26.47%) were undernourished, and the rest were normal for age.

Regardless of etiology, most patients with bacterial meningitis have similar clinical syndromes.

Fever, a hallmark of infection, generally is present. In this study, the mean days of fever before admission was four days.

Signs of meningeal inflammation may be minimal in the infant, but irritability, restlessness and poor feeding may be noted. In this study, irritability was noted in fifteen patients (44.1%), while poor suck was noted in five (14. 7%).

Increased intracranial pressure occurs due to cell death, increased capillary vascular permeability, and increased hydrostatic pressure secondary to obstructed reabsorption of CSF in the arachnoid villi or obstruction of CSF flow from the ventricles[1]. Increased intracranial pressure manifests as headache in order children and a

bulging fontanelle in infants. In this study, eighteen of the thirty four patients studied (52.9%) had a bulging anterior fontanelle at the time of admission. Six patients (17. 6%) had vomiting as a sign of increased intracranial pressure.

Focal neurologic signs may be present at the time of admission and was a poor prognostic sign and could be correlated with persistent abnormal neurologic examinations. In this study, of the three patients (8.8%) who presented with focal neurologic deficits. None died, although two were hydrocephalic and one was spastic at the time of discharge. Of these three, one was admitted at the intensive care unit for close monitoring. There was a highly significant association between neurologic signs and the occurrence of late afebrile seizures[14], and this could be explored in future studies.

Papilledema occurs secondary to venous sinus occlusion, subdural empyema, or brain abscess. In this study, it was observed in only one patient who died in less than twenty four hours.

Seizures before admission occur in about 20% of children with bacterial meningitis and during the first or second day in the hospital in about 26% of cases. Green and colleagues[13] found that 111 of 410 (27%) children with bacterial meningitis had seizures at or before the time of diagnosis. In this study, ten of the subjects (29.41%) had seizures which were generalized in character and was the reason why medical consultation was sought.

In the similar study by Green, seizures noted before or during the first several days hospitalization were of no particular prognostic significance. Their occurrence did not herald the development of a permanent seizure disorder.

Seven percent of patients with bacterial meningitis have focal or generalized seizures three months to fifteen years after recovery[14]. In this study, of the patients who presented with seizures at the time of admission, seven (29.59%) still had seizures at the time of discharge.

Seizures before admission have correlated positively with abnormal audiometric studies and permanent hearing handicaps. Although this study aimed at looking into this, by chart review alone, it is difficult to determine which among the patients really had hearing loss as a sequelae of pneumococcal meningitis.

Hydrocephalus develops and is the result of adhesive thickening of the arachnoid about the cisterns at the base of the brain. In this study, thirteen of the thirty four patients (38.2%) had hydrocephalus as evidenced by a head circumference more than the 90% percentile for age, and or cranial ultrasound findings of hydrocephalus at the time of admission.

Xanthochromia is a characteristic finding in CSF of patients with bacterial meningitis, and hemorrhage or an elevated protein concentration in CSF may be associated with xanthochromia. This finding is supported in this study where a xanthochromic CSF was noted in almost all of the patients studied.

Raised CSF protein levels were due to increased vascular permeability of the blood brain barrier and the loss of albumin-rich fluid from the capillaries and veins traversing the subdural space. Hypoglycorrhachia was due to decreased glucose transport by cerebral tissue across the inflamed choroids plexus and from increased utilization of glucose by host tissue[2].

The normal CSF of children 3 months of age or older contains fewer than 6 white cells mm^2 and 95% of children in this age group have no polymorphonuclear cells, thus the presence of a PMN in the CSF may be regarded as abnormal. In this study, more than two thirds of the subjects had WBC counts of less than or equal to 250 in the CSF. More than of the subjects had protein levels of <3 and more than half had sugar levels between 1-10%. One third had a polymorphonuclear count form 21-40.

Meningeal exudates may be distributed cerebral veins, venous sinuses, convexity of the brain, cerebellum, sulci, sylvian fissures, basal cistern, and spinal cord. This explains why ventriculitis may be present, as may subdural effusions, and empyema although rare.

Subdural effusions occur frequently during the course of meningitis although the exact pathogenesis is not known. The high incidence of effusion and the fact that subdural fluid collections may be found early in the course of bacterial meningitis in children suggest that subdural effusions should be considered a concomitant of meningeal inflammation rather than a complication of the disease. This occurs because numerous veins traverse the subdural space and inflammation of these and of the dural capillaries could produce an increase in vascular permeability and loss of albumin-rich fluid into the subdural space. Collection of fluid in the subdural space occurs in fact in about 50% of infants and children during acute illness[15]. There was no greater incidence of nuerologic sequelae or developmental delay on long-term follow-up in patients with effusion, compared with those who did develop effusion[16]. In this study, of the four (11.76%) patients who developed

effusion during the course of the illness, all were noted to have nuerologic sequelae at the time of discharge which included hydrocephalus in three patients (75%), seizures in two (50%), and spasticity in two (50%).

Subdural empyema as opposed to effusion occurs rarely and as reported by Smith and Landing occurred only in 1 of 34 patients[16]. In this study six of the thirty four patients studied (17.65%) developed this complication.

The *Pneumococcus* causes one of the most severe forms of meningitis and 20 to 30% of patients will die from the condition. The death rate was highest in very young or very old patients, and those with other serious medical conditions. Patients who were comatose when they reached the hospital have a very poor prognosis. Although death usually occurs rapidly, some patients died despite several days of appropriate antibiotic treatment. The reason for their failure to respond to treatment was uncertain. It had been estimated that about 50% of survivors will have some degree of lasting brain damage which may include deafness, weakness or epilepsy. Some of these complications were mild and will slowly improve after weeks or months. Many patients however were left permanently disabled.

In this study, it was noted that patients who were comatose and critically ill on admission were treated with a third-generation cephalosporin. It was further observed that their clinical course was complicated by nosocomial sepsis and ventilator associated pneumonia. This could explain why the length of treatment in the ampicillin-chloramphenicol group was shorter than those shifted from ampicillin-chloramphenicol to a cephalosporin, or those started with ceftriaxone or cefotaxime from start.

Observational studies over the past 20 years have suggested that delay in antibiotic administration affects the clinical outcome of patients with bacterial meningitis. However, most of those studies failed to acknowledge that a number of other variables can also affect clinical outcome. These variables include pathogen virulence, patient comorbidities, and severity of disease at the time of presentation. Therefore, the independent impact of treatment delay could not be accurately assessed[4].

The prognosis in individual patients with bacterial meningitis depends upon factors, including the following: (1) age of the patient, (2) the time course or progression of illness before effective antibiotic therapy, (3) the specific microorganism causing the disease, (4) the number of organisms, (5) the rapidly with which CSF was sterilized after initiation of antibiotic therapy, and (6) the presence of disorders that may compromise host response to infection[17].

The younger the patient and the greater the antigenic load at the time of admission, the worse the prognosis. Bacterial colony counts appear to be a more reliable indicators sequelae than antigen concentration. Seizure, subdural effusions, bacteremia, and a more prolonged fever were more frequent in children who have more than 107 CFU/ml of a particular organism in CSF at the time of admission[18]. Children with colony counts equal to or greater than 107 cfu/ml also are significantly more likely to experience hearing loss and speech disturbance than were children with meningitis but lower concentrations of bacteria within CSF specimens.

The greatest morbidity after bacterial meningitis occurred in individuals affected between birth and four years of age[10]. In this study, of the six patients who died (17.65%), five (83.33%) were less than or at least a year old.

In one large prospective study as reported by Feigin, 32.8% of children had abnormalities detectable on neurologic examination at the time of discharge but by 5 years after discharge, specific deficits were noted in only 11.1% of the total group[11]. As a result of the late seizures in some of these patients, the frequency of neurologic sequelae 15 years after discharge was 14%[14]. Shortly after discharge, hemiparesis or quadriparesis was noted in 30 patients (12.4% of the total group), but at one year after discharge, paralysis was noted in only 5. These data reflect the tendency for even major neurologic defects to clear unpredictably with time.

In this study, of the 34 patients studied, twenty six (76.4%) had neurologic sequelae at the time of discharge. Six (17%) had persistent tone, seven (20.6%) had persistent seizures, and thirteen (38.24%) had hydrocephalus, one of which underwent ventriculoperitoneal shunting during the same admission. The presence of visual problems and clinically significant hearing deficit can not be ascertained in this study by review of records alone.

CONCLUSION

Pneumococcal meningitis is one of the most severe forms of meningitis in children. It occurs predominantly in those less than one year old. And in

this study, no sex predilection was observed. The most common presenting sign was seizures which was the primary reason for medical consultation. Other manifestations include signs of upper respiratory tract infection such as cough or colds, increased tone, irritability, bulging anterior fontanelle, and nuchal rigidity. The most common predisposing factor in the development of pneumococcal meningitis remains to be pneumonia, followed by upper respiratory tract infection. Cerebrospinal fluid analysis reveals pleocytosis with segmenter predominance, and cranial ultrasounds findings were abnormal and show meningitic changes in majority of cases.

Outcome was not significantly different among the treatment groups in this study although the duration of hospital stay was significantly different among the three groups, with length of treatment in the ampicillin-chloramphenicol group significantly shorter than those shifted from ampicillin-chloramphenicol to a third-generation cephalosporin.

The most common neurologic sequelae in patients with pneumococcal meningitis was the development of hydrocephalus followed by seizures.

Based on this study, Ampicillin-Chloramphenicol combination was used as initial empiric therapy in the treatment of pneumococcal meningitis. The decision to shift antibiotics was influenced by the clinical course of the patient, objective laboratory parameters, and development of sequelae.

RECOMMENDATION

Seizures before admission have correlated positively with abnormal audiometric studies and permanent hearing handicaps. Although this study aimed at looking into this, by chart review alone, it was difficult to determine which among the patients really had hearing loss as a sequelae of pneumococcal meningitis, and further objective studies are needed to document this. The same is true in determining the presence of visual problems, and learning handicaps as a sequelae of meningitis.

There was a highly significant association between neurologic signs and the occurrence of late afebrile seizures, and this could likewise be explored in future studies.

References

1. Behrman RE, Kliegman RM, Jenson HB: Nelson's Textbook of Pediatrics 16th Edition. W.B. Saunders Company, 2002.
2. Feigin, et. Al. (1998) Bacterial meningitis beyond the neonatal Period. Textbook of Pediatric Infectious Diseases 1:404-429.
3. Baumgartner, et.Al. (1983) Bacterial meningitis in order neonates. *Am. J. Dis. Child.* 137: 1052-1054.
4. Aronin,et.Al. New perspectives on Pneumococcal meningitis.
5. Davey, et.Al. (1982) Bacterial meningitis - Ten years' experience. 88:383-401.
6. Klass, et.Al. (1992) Therapy of bacteria sepsis, meningitis, and otitis media in infants and children: 1992 poll of directors of programs in pediatric infectious diseases. *Pediatric Infectious Disease Journal* 11:702-705.
7. Word, et. At (1998) Current therapy of bacterial sepsis and meningitis in infants and children: A poll of directors of programs of pediatric infectious diseases. *Pediatric Infectious Disease Journal* 7:267-270.
8. Hansman, et. Al (1967) A resistant pneumococcus. Lancet 2:264-265.
9. Naraqui et. Al (1974) Relapsing pneumococcal meningitis: Isolation of an organism with decreased susceptibility to penicillin. *J. Pediatrics* 85:671-673.
10. Fraser et. Al. (1975) Undiagnosed bacterial meningitis in Vermont children. Ann. U. Epidemiol 102:394-399.
11. Feigin, R.D., and Dodge,P.R.: Personal experience: Unpublished data for prospective studies of bacterial meningitis, 1974-1979.
12. Feigin, R.D and Shearer, W.T.: Opportunistic infection in children. Part 1. in the compromised host. *J. Pediatrics.* 87:507-514, 1975.
13. Green S.M, Ronthrock, S. G., Clem, K.J. et. Al.: Can seizure be the sole manifestation of meningitis in febrile children? *Pediatrics* 92:527-534, 1993.
14. Pomeroy, S.L., Holmes, S.JI, Dodge, P.R., et. AL.: A prospective evaluation of the neurologic sequelae of bacterial meningitis in children with special emphasis on late seizures. *N. England Journal of Medicine.* 323:1651-1657,1990.
15. Dodge, P.R., and Schwartz, M.N.,: Bacterial meningitis: A review of selected aspects, II. Special neurologic problems, postmeningitic complications and clinicopathologic correlations. *New England Journal of Medicine.* 272:1003-1010,1965.
16. Smith, A.L.,: Neurologic sequelae of meningitis. *New England Journal of Medicine.* 319:1012-1014, 1988.
17. Lebel, M.H., and McCracken, G.H., Jr.: Delayed cerebrospinal fluid sterilization and adverse outcome of bacterial meningitis in infants and children. *Pediatrics* 83:161-167, 1989.