Outcome of Bacterial Meningitis in Children age 1 Month – 12 Years in a Public Sector Hospital Treated with 1st line Antibiotics

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Abstract

Objective: To determine the effectiveness of using first line antibiotics for the treatment of acute bacterial meningitis in children admitted in a public sector hospital and assessing its outcome with the help of data by need for using second line antibiotics therapy and length of stay in hospital.

Method: This Crosssectional study was conducted at department of Pediatrics, Pakistan Institute of Medical Sciences, Islamabad over a period of 6 months from January 2019 to July 2019. All children between the age of 1 month – 12 years, of both genders admitted in pediatric ward with acute bacterial meningitis, based on clinical features plus CSF findings, were enrolled in the study. These children were started with first line antibiotic therapy after admission in ward which included ceftriaxone alone or a combination of ampicillin and cefotaxime or cefotaxime plus amikacin depending on age specific recommendations for that age group. All children were closely observed in ward for improvement or deterioration of symptoms. If there was deterioration of symptoms, then second line antibiotics were started which in our case was vancomycin combined with ceftriaxone or meropenem combined with vancomycin. Duration of hospital stay was also noted. Data was analyzed by SPSS version 22.

Results: A total of 51 patients were enrolled in the study. Mean age of children in the study was 3.23 ± 3.3 years. There were 33(65.1%) males and 18(34.9%) females. Only 30(58.6%) children were completely vaccinated, rest were either partially vaccinated or not vaccinated at all.]In the first line antibiotics course, ceftriaxone was the most common antibiotic, which was prescribed to 32(61.3%) children, followed by a combination of cefotaxime with amikacin 13(23.7%) and ampicillin plus cefotaximeto 6(4.3%). Second line therapy was needed in only15(29%) children. The commonly prescribed was a combination of vancomycin and meropenem. The total duration of stay in hospital was for 10-14 days.

Conclusion: Our study concluded that first line antibiotic therapy is still an effective treatment for acute bacterial meningitis. So, in the wake of emerging antibiotic resistance, irrational use of antibiotics should be avoided.

Keywords: Acute bacterial meningitis, first line antibiotics, second line antibiotics, antibiotic resistance.

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Introduction

Acute bacterial meningitis is one of the major causes of febrile illnesses in childhood.[1] It is still a major cause of morbidity & mortality in infants and children of age less than five years. Each year, in Pakistan about 23000 children die because of acute bacterial meningitis.[2] Acute bacterial meningitis results from hematogenous dissemination of microorganisms from a distant site of infection. More than sixty percent cases of meningitis develop during first two years of

life, owing to weak immune system, partial vaccination, and high vascularity of the brain.[3] The clinical presentation of bacterial meningitis is often vague in infants and children because of the immaturity of central nervous system in less than five years age, so there should be a high index of suspicion.[4] Acute bacterial meningitis therefore should be considered as a neurological emergency and early treatment with intravenous antibiotics is highly recommended. If left untreated, mortality may approach 100% but with recent developments in antibiotic preparation and with advanced intensive care, the meningitis related mortality has been reduced to approximately 5-10%. Worldwide, the risk of neurological sequelae in survivors of acute bacterial meningitis approaches 20%.[5]

Most common etiological organisms are streptococcus pneumoniae, Hemophilus Influenzae type b, Neisseria meningitides, group B streptococcus, E. coli and Listeria monocytogenes. Since the introduction of Hib and pneumococcal conjugate vaccine, there is an overall reduction in incidence of acute bacterial meningitis. However, the mortality from acute bacterial meningitis remains substantial and the case fatality rate did not change.[6] Slack M et al reported in 2015 that Hib still accounts for >29,000 deaths worldwide in children of age <5 years, while up to 40% children can suffer from permanent disabilities. It is therefore essential for clinicians to recognize the clinical signs and symptoms of bacterial meningitis and perform cerebrospinal fluid examination to confirm the diagnosis of meningitis. Although for confirmation of diagnosis of acute bacterial meningitis, the microbiological culture of the cerebrospinal fluid (CSF) is considered to be the gold standard.[8] However, this method is time-consuming and furthermore, there is low bacterial growth owing to prior antibiotic use. Moreover, the sensitivity of culture is also seriously hampered by use of antibiotics prior to cultures (both blood and CSF). Emergence of microbial resistance has further added to the complexity of managing this problem. Therefore, where available, use of PCR (polymerase chain reaction) can give rapid results and is also sensitive. This can improve the speed and accuracy of detection of pathogens like Hib and pneumococcus.[9]

Treatment of bacterial meningitis depends largely on using intravenous antibiotics targeted to the suspected organism according to prevalent organism for each age group and generally involves a treatment with third generation cephalosporin. Special consideration is given to the ability of drug to cross the blood brain barrier. Despite antibiotic therapy numerous patients experience severe neurologic complications and sequelae.[10] To decrease morbidity and mortality; clinicians therefore are jumping to 2nd and 3rd line antibiotics in the absence of culture sensitivity reports. This in return is further adding to the problem of increasing antimicrobial resistance. Present study therefore was conducted to determine the effectiveness of 1st line antibiotics in treating acute bacterial meningitis in children admitted in a public sector hospital.

Material and Methods

This cross- sectional analytic study was conducted in department of Paediatrics, Pakistan Institute of Medical Sciences Islamabad over a period of 6 months from January 2019 to July 2019. 51 patients of both genders, between ages of 1 month till 12 years admitted in pediatric medicine ward during the study period with signs and symptoms and positive CSF findings suggestive of meningitis were enrolled in the study. Non-probability, consecutive sampling technique was used. Children with diagnosis of recurrent bacterial meningitis, children already receiving oral or intravenous antibiotics treatment for this illness, and children with spinal malformation and hydro-cephalous were not included in the study. Children presenting with fever, fits, altered state of consciousness, having a bulging fontanelle, increased body tone, neck stiffness, positive Kernig's or Brudzinski sign plus positive CSF findings were assigned the diagnosis of acute bacterial meningitis. A total of 51 patients fulfilling the inclusion criteria, were enrolled in the study. Ethical approval was taken from IRB. Informed consent was taken from parents before enrollment of the child in the study and before performing lumbar puncture. Demographic details were recorded in the proformas for the study purpose. Children were then started with first line antibiotic therapy according to the recommendations for that age group which included ceftriaxone alone or a combination of ampicillin with cefotaxime or cefotaxime with amikacin. All children were closely observed in pediatric ward for progression or resolution of signs and symptoms. If symptomsdo not improve within 48-72 hours of starting intravenous antibiotic therapy, then second line antibiotics were started. Second line antibiotics in our study included addition of vancomycin with ceftriaxone or a combination of vancomycin with meropenem. Improvement of general condition of child, duration

of hospital stay and any complication during stay in hospital for treatment purpose were also noted in the proforma along with report of cerebrospinal fluid including biochemistry, cytology and culture.

Data was analyzed by using SPSS v. 22. Gender, duration of hospital stay, antibiotics, steroid use and vaccination status were presented as frequency and percentage. Age, CSF findings were presented as mean ± Standard deviation.

Results

The mean age of children included in the study was 3.23±3.31 years. There were about 25(47.8%) children of age <1 year, 12(24.2%) children were of age 1-5 years while 14(28.0%) were of age > 5 years (up to 12 years). There were 33(65.1%) males and 18(34.9%) females (Table-1). Complete vaccination was done in only 20(39.2%) children while 31(60.7%) children had either incomplete vaccination or not vaccinated at all. First line antibiotics were started according to age specific recommendations (Table 2). Among them, Ceftriaxone was the most common antibiotic, which was prescribed to 32(62%) children, while a combination of cefotaxime with amikacin was prescribed to 13(25.4%) and a combination of ampicillin and cefotaximeto 6(11.7%) children (Table 2).

Second line therapy was given to only 15 children. The most commonly prescribed was a combination of vancomycin and meropenem 8(15.6%), followed by a combination of ceftriaxone and vancomycin to 3(5.8%) children. Tanzobactum and cefepime were prescribed to 4(7.8%) children. In addition to antibiotics steroids were given to 38 (52.7%) children as a part of treatment of meningitis. (Table-2) Out of 51 children, 18(35.2%) stayed at the hospital for >14 days while 33(64.7%) children stayed for <14 days in the hospital. (Fig-1)

Table 1: *Characteristics of children with bacterial meningitis*

Demographic detail	Total(N=51)	Percentage
Age		
1 month-12 months	25	(47.8%)
1-5 years old	12	(24.2%)
> 5 years	14	(28.0%)
Gender		
Male	33	(65.1%)
Female	18	(34.9%)
Vaccination status		
Completely vaccinated	20	(39.2%)
Incomplete/no vaccination	31	(60.7%)

Table 2: *Distribution of First Line and Second Line Antibiotics.*

First line antibiotics	Total(N=51)	percentage
Ceftriaxone	32	(62.7%)
Cefotaxime + Amikacin	13	(25.4%)
Ampicillin + cefotaxime	06	(11.7%)
Second line antibiotics		
Vancomycin + Meropenem	8	(15.6%)
Vancomycin + Ceftriaxone	3	(5.8%)
Tanzo/ cefepime	4	(7.8%)
Steroids		
Given	38	(74.5%)
Not given	13	(25.4%)

Table 3: *Age wise distribution of first line antibiotics.*

Age	Choice of 1st line antibiotic
1-2 months	Cefotaxime + Amikacin
2-3 months	Ampicillin + cefotaxime
> 3 months age	Ceftriaxone

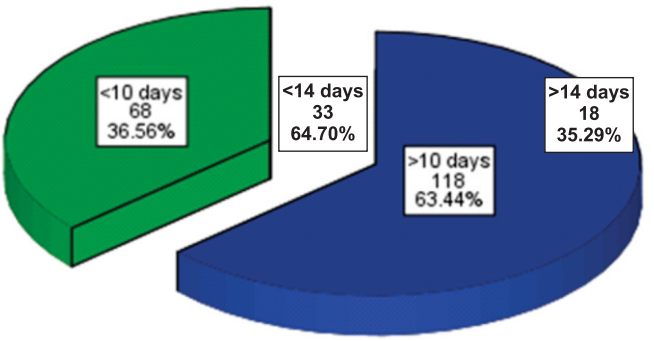

Fig 1: *Distribution of Hospital Stay*

Discussion

The invention of antibiotics has significantly improved the outcome of patients with severe infections. Antibiotics discovery has also improved the prognosis of several infectious diseases and outcome of surgical procedures. The capability of antibiotics to cure and prevent infections has considerably improved the quality of life and has decreased mortality rate significantly along with improving the morbidity. However, the injudicious and extensive use of antibiotics, especially when available over-the-counter and where not indicated

has caused the emergence of multi-drug resistant bacterial strains. These emergent bacterial strains fail to respond to the conventional antibiotic therapies.[12] This is an emergency health concern which poses a threat noticeably in low and middle income countries because of easy availability of antibiotics and poor regulations by the government.[13] Many general practitioners (GPs) and unlicensed health care providers prescribe broad spectrum antibiotics even for mild, self-limiting infections and viral illnesses.[14] World health organization (WHO) has thus placed antibiotic stewardship program at the heart of its Global Action Plan to curb antibiotic resistance.[15] Recently, a significant increase has been noticed in these pathogenic strains, which thus limits the choice of antibiotics against severe infections. Antibiotics are essential for the success of certain commonly performed surgical procedures which includes gynecological and orthopedic along with general surgeries and transplant procedures. The resistance to antibiotics is growing in all type of pathogens, particularly noticeable are methicillin resistant staphylococcus aureus and salmonella typhi.

In our study, there were 33(65%) males and 18 females (34%), which were comparable to another study where males were more affected with bacterial meningitis. This can be attributed to good immune status of females.[16] Predominant age group of children affected in our study was of less than 1 year 25(47.8%) which are comparable with another study which showed that patients of extreme ages are more affected with bacterial meningitis owing mainly to their weak immune system. Also children in this group are mostly unvaccinated or partially vaccinated owing to multiple factors.[17]

Our study showed that microorganisms are susceptible to 1st line antibiotics as 2nd line antibiotics were used in only 15(29%) patients. Our results of good response to first line antibiotics are comparable with another study which showed that pneumococcal isolates were not found resistant to ceftriaxone and vancomycin.[18] Although in our study very few bacteria were isolated so sensitivity of antibiotic spectrum could not be assessed with certainty but clinical response to first line antibiotics was very good.

However, our results of good response to first line antibiotics are in contrast to the list published by world Health Organization in 2017 in which it has placed H. Influenzae and streptococcus pneumoniae in medium priority list 3 of pathogens in need of new antibiotics.[19] This can be attributed to the overuse of extended spectrum of cephalosporins. Study by H Bilal et al also shows resistance of E. coli to ampicillin and 100% susceptibility to colistin and 92% to meropenem.[20] This is a point of concern as these antibiotics (colistin and meropenem) are considered third line or sometimes fourth line antibiotics.

Development of antibiotic resistance by Enterobacter species causes a high mortality, prolonged hospital stay, and increased cost of treatment involved during the hospital stay. Resistance of Enterobacter species should thus be primarily minimized.[21,22]

After several years of discovery and use of antibiotics against infection control, bacterial infections are again becoming a great risk, owing largely to unnecessary use. We are threatening their availability for our future generations so that they can enjoy infection free atmosphere.[23] The crisis of antibiotic resistance occurred due to the overuse as well as misuse of antibiotics, coupled to the lack of development of new antibiotics by pharmaceutical industry owing mainly to the decreased economic incentives and thought-provoking regulatory requirements.[24] A combination of dropping profits, monitoring system by government and inappropriate and inadvisable use of antibiotics by clinicians is hereby-leading to this alarming situation.[25]

Conclusion

Thus in our study, first line antibiotic therapy was effective in 80.6% cases and the need for second line therapy was needed in only 29.4%. Thus to prevent the emergence of antibiotic resistant strains, it is recommended to start empirical treatment with first line antibiotics which can later be changed according to the response to treatment and culture sensitivity reports. Every hospital should develop SOPs (standard operating protocols) for starting the first line and second line antibiotic regimens which should be practiced in their hospital for treating severe infections in admitted patients.

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Authors Contribution

AA: Conceptualization of Project
TB: Data Collection
AK: Literature Search
TB: Statistical Analysis
HA: Drafting, Revision
HRS: Writing of Manuscript