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Original Research Article

Analysis of outcome of acute encephalitis syndrome after inclusion of coverage against scrub typhus

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ABSTRACT

Background: Acute encephalitis syndrome (AES) has emerged as a major epidemic in Bihar and is associated with high mortality. Owing to the increasing burden of disease and its associated morbidity and mortality, studies were undertaken to evaluate specific etiology of AES. Some studies suggested emergence of scrub typhus as a major cause of AES accounting for about 25% of the cases1. A Standard Operating Procedure (SOP) was developed for treatment of AES cases in Bihar which included addition of Injection Azithromycin (@ 10 mg/kg for 7 to 10 days in case of suspected mycoplasma/rickettsial infection. The objective of the study is to compare the outcome of AES before and after the inclusion of coverage against rickettsial infection.
Methods: It is a randomized controlled trial conducted in the Department of Pediatrics, Patna Medical College and Hospital, Patna from January 2016 to August 2018.
Results: Total number of patients enrolled in both the groups were 127 and 88 respectively. No significant difference were seen in the baseline socio- demographic characteristics of the two groups. Case Fatality Rate in the 1st group (without inclusion of Azithromycin) was 39.3% while in the 2nd Group (with Azithromycin) was 12.5%.
Conclusions: Due to the emergence of scrub typhus as a major etiological factor for AES, inclusion of coverage against it along with measures like widespread immunization against Japanese Encephalitis and prompt management of complications and euglycemia, can result in steady decline in the death rates due to AES.

Keywords: Acute encephalitis syndrome, Azithromycin, Scrub typhus, Standard operating procedure

INTRODUCTION

Acute encephalitis syndrome is defined as a person of any age, at any time of year with acute onset of fever and a change in mental status (including symptoms such as confusion, disorientation, coma or inability to talk) and/ or new onset of seizures, excluding simple febrile seizures. Acute encephalitis syndrome (AES) has emerged as a major epidemic in Bihar and is associated with high mortality.

Owing to the increasing burden of disease and its associated morbidity and mortality, studies were undertaken to evaluate specific etiology of AES. One of the study conducted by the Department of Microbiology of Patna Medical College, Patna along with King George's Medical University, Lucknow, observed that the positivity rates of Scrub typhus IgM or PCR was 25%, followed by IgM positivity for Japanese Encephalitis 8.1%, West Nile Virus (6.8%), Dengue virus (6.1%), Chikungunya Virus (4.5%).[1] Based on similar observations from other studies (2,3,4,5).

A Standard Operating Procedure (SOP) was developed for treatment of AES cases in Bihar which included addition of Injection Azithromycin (@ 10 mg/kg for 7 to 10 days in case of suspected mycoplasma/rickettsial infection.

METHODS

The study was conducted in Patna Medical College and Hospital, Patna, Bihar. Case presenting with clinical diagnosis of AES as per WHO, from January 2016 to August 2018, admitted in Patna Medical College were enrolled in the study.

Inclusion criteria

- Age between 0- 15 years
- Acute onset of Fever
- Change in mental status
- Seizures
- Neurologically normal before the onset of fever.

Exclusion criteria

- Known case of seizure disorder
- Fever for longer duration
- Febrile convulsion
- Cerebral palsy.

The study was approved by Institutional Ethical Committee of Patna Medical College and Hospital, Patna.

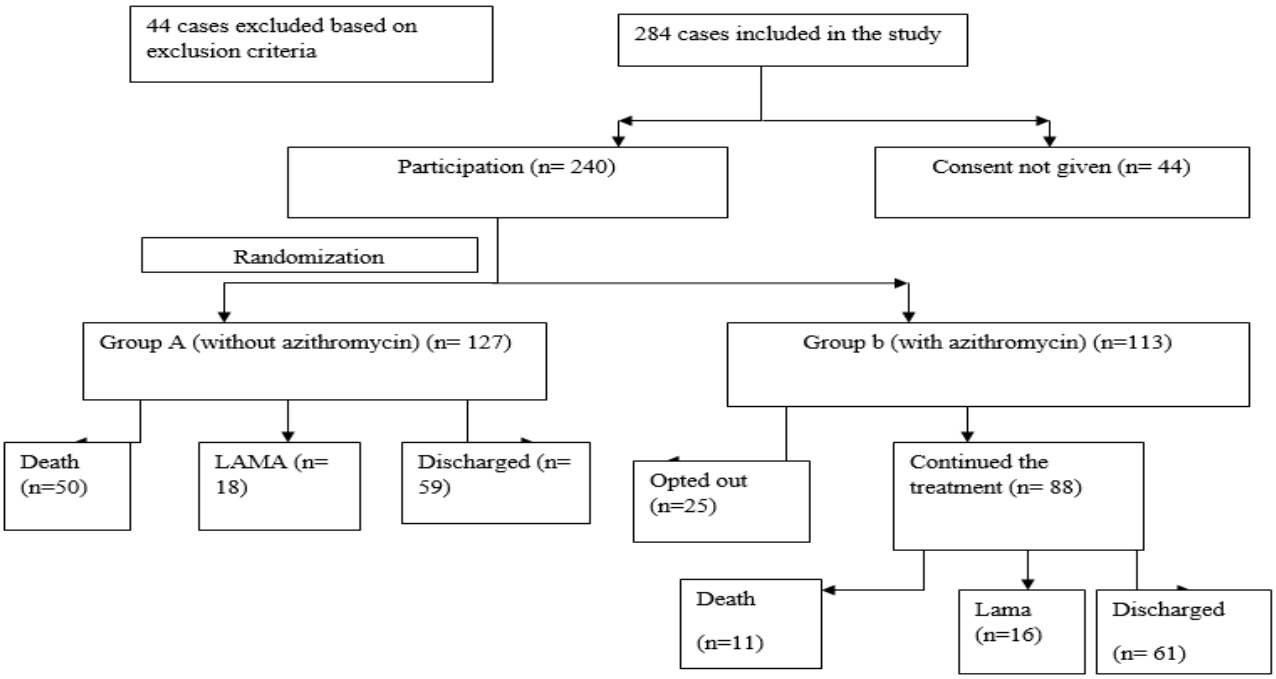

Figure 1: 328 cases of suspected AES were admitted in the given time period.

Study type

It is a randomized controlled trial conducted in the Department of Pediatrics, Patna Medical College and Hospital, Patna from January 2016 to August 2018. All cases which presented with acute onset of fever and a change in mental status including symptoms such as confusion, disorientation, somnolence with or without convulsion were included in the study, details of the treatment were noted, and analysis of outcome was done.

Statistical analysis

All statistical analysis were done using SPSS version 18.0 software and CDC Epi Info Software. Intergroup comparisons of categorical and continuous variables were done using Fischer Exact's test and Chi square tests respectively.

RESULTS

The final enrolment of patients in Group A (without Azithromycin) was 127. Mean age of presentation in this group was 5.73 years. Male to Female ratio was 1.35. 72 cases belonged to rural background and 55 cases belonged to Urban background.

In Group B, the total enrolment was 88, and the mean age of presentation was 6.07 years. Male to Female Ratio in this group was 1.58. Cases from Rural and Urban

background were 45 and 43 respectively. p value for these baseline characters were more than 0.05, showing that there was no significant difference between the two groups.

In Group A, 50 patients expired, 59 were discharged and 18 patients Left Against Medical advice. Case Fatality Rate in this group was 39.3% (Table 1) In group B, 11 patients expired, 61 got discharged and 16 Left against Medical advice.

Case Fatality Rate in this group was 12.5%. p value for death and discharge in the two groups were less than 0.05 suggesting that there was significant reduction in mortality rates with inclusion of azithromycin.

Table 2 shows age wise stratification of the cases. Of the 30 patients belonging to the age group 0-2 years in Group A, 19 were male and 11 were female, 29 patients of age group 2-5 years (sex ratio =1.23) and 68 patients were of more than 5 years (sex ratio = 1.26).

In group B, 14 cases belonged to age group 0-2 years (Sex ratio =1.33), 25 cases from 2-5 years (sex ratio= 1.08) and 49 patients were of more than 5 years. (Sex Ratio= 2.06). The p value of the age wise stratification was more than 0.05, showing that there was no significant difference between the two groups. Similar results were seen for age wise stratification of urban and rural patients.

Table 1: Socio demographic characteristics of the two groups.

	Without azithromycin (n=127)	With azithromycin (n=88)	p value
Age (in years)			
Mean age (SD)	5.73 (2.49)	6.07 (2.84)	0.3539
Sex			
Male	73	54	0.57
Female	54	34	
Background			
Rural	72	45	0.50
Urban	55	43	
Outcome			
Death	50	11	0.0001
Discharge	59	61	0.001
Lama	18	16	
Case fatality rate	39.3%	12.5%	

p value= probability test

Table 2: Age wise stratification.

	Without azithromycin (n=127)		With azithromycin (n=88)		p value
Age (in years)	**Male**	**Female**	**Male**	**Female**	
0-2 years	19	11	08	06	0.951
2-5 years	16	13	13	12	0.817
>5 years	38	30	33	16	0.28
Age (in years)	**Rural**	**Urban**	**Rural**	**Urban**	
0-2 years	16	14	06	08	0.74
2-5 years	18	11	14	11	0.78
>5 years	38	30	25	24	0.70

Table 3: Outcome of the two groups in specific age groups.

	Without azithromycin				With azithromycin				
Age	**Lama**	**Exp**	**Disch.**	**CFR**	**Lama**	**Exp**	**Disch**	**CFR**	**P value**
0-2 years	05	12	13	40%	02	02	10	14.2%	0.08
2-5 years	04	11	14	37.9%	05	02	18	8%	0.01
>5 years	09	27	32	39.7%	09	07	33	14.2%	0.003

CFR: Case fatality rate, Disch: Discharge, Exp: Expired, LAMA= Left against medical advice

In the first Group, 30 cases belonged to age group of 0- 2 years, out of which 13 got discharged and 12 expired. Case Fatality Rate in this group was the highest which was 40%. Case Fatality rate in the same age in Group B was 14.2%. Although there was significant reduction in the case fatality rate in this age group, p value was not significant.

In the age group of 2-5 years, case fatality rate was 37.9% in group A and 8% in Group B, having a

significant p value. Reduction in Case fatality rate was also significant for the age group of > 5 years (Table 3)

DISCUSSION

AES is a major seasonal health problem in Bihar. Studies conducted by the Department of Pediatrics and Department of Microbiology of Patna Medical College, Bihar in association with Department of Microbiology in King George's Medical College, Lucknow suggested the emergence of Orientia tsutsugamushi as an important cause of Acute Encephalitis Syndrome in this region.[1]

In similar studies conducted in Assam, O.tsutsugamushi DNA was detected in 8.6% to 12% cases admitted with symptoms of AES. The case fatality rate was around 49%.[2]

The National Vector borne disease Control Program reported > 60 000 cases of Acute encephalitis syndrome in India during 2010-2016; 8 states (Assam, Uttar Pradesh, West Bengal, Odisha, Tamil Nadu, Karnataka, Manipur, and Tripura) accounted for most of the cases.[3]

O.tsutsugamushi has already been established to invade Central nervous system.[4] In a recent prospective study from Laos, O. tsutsugamushi was detected in 12% patients with CNS infection.[5]

The high prevalence of illness and death resulting from scrub typhus can be attributed to various reasons. First, because JE Virus is the predominant etiological agent of AES in this region. Health providers usually do not suspect other etiological factors, including scrub typhus. Also, nonspecific clinical features of scrub typhus, i.e. absence of eschar/rash lead to diagnostic dilemmas. Treatable infections like scrub typhus are grossly underestimated because of low index of suspicion and limited diagnostic facilities. Proportion of deaths due to untreated scrub typhus varies across different regions from 30% to 70%.[6-8] The absence of distinguable clinical features among AES identifying etiological factors makes differential diagnosis difficult, and thus conditions remain untreated. The clinicians are unaware of the presence of disease and it remains a major hindrance in the recognition and successful treatment of the condition.

In a meta-analysis, comparative effectiveness of azithromycin for treating scrub typhus, by Lee SC et al, in 2017, it was concluded that Azithromycin was as effective as Doxycycline (which is contraindicated in pregnant women and children) with higher treatment success rates, lower adverse effects, and, therefore, can be used as a first line against scrub typhus.[9]

In the present study, mean age of presentation in both the groups were 5.73(+2.49) and 6.07 (+2.84) respectively. Similar study was conducted in Delhi with mean age of presentation was 5.8+3.5 years.[10] Male to Female ratio in the two groups were 1.35 and 1.58. Other studies conducted also showed male predominance with ratio of 1:27.

Case fatality rate in present study before inclusion of coverage against Scrub Typhus was 39.3% and after inclusion of coverage against Scrub typhus was 12.5%. The Case Fatality rate of AES in various studies ranges from 30% to 70%.

CONCLUSION

Due to the emergence of scrub typhus as a major etiological factor for AES, inclusion of coverage against it along with measures like widespread immunization against Japanese Encephalitis and prompt management of complications and euglycemia, can result in steady decline in the death rates due to AES. Despite the best efforts by the health personnel, AES continues to be a major cause of mortality in Bihar. More comprehensive studies need to be undertaken to elaborate the etiology of AES.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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