

Research Article**Comparative study between intramuscular ceftriaxone and oral amoxicillin in term of efficacy in cases of uncomplicated severe acute malnutrition**

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ABSTRACT

Objective: To compare the efficacy of two days intramuscular ceftriaxone versus five days oral amoxicillin in the treatment of uncomplicated severe acute malnutrition.

Material and methods: This randomized controlled was conducted at Department of Pediatrics Jinnah Hospital, Lahore from January 2017 to June 2017. Total 70 patients with uncomplicated severe acute malnutrition age range from 6-59 months either male or female were selected for this study.

Results: Meant age of the patients was 29.76 ± 16.919 years, mean age of patients of group A was 29.17 ± 17.578 years and group B was 30.34 ± 16.469 years. Efficacy of treatment was noted in 25 (71.43%) patients of group A and in 16 (45.71%) patients of group B. Statistically higher rate of efficacy of treatment was noted in study group A as compared to study group B with p value 0.05. Statistically significant difference of efficacy between the male patients of both groups was noted with p value 0.0014. But insignificant difference of female patents of both groups was detected.

Conclusion: Results of this study showed significantly higher rate of efficacy in patients of acute malnutrition treated with ceftriaxone IM for 2 days as compared to oral amoxicillin for 5 days. Male patients of ceftriaxone group found with higher rate of efficacy as compared to male patients of amoxicillin group but insignificant difference was noted in female patients of both study groups. There was insignificant association between age and efficacy was noted.

Key words: Malnutrition, Infection, Antibiotics, Pneumonia, Sepsis, Diarrhoea

INTRODUCTION

Malnutrition is one of the important causes of mortality and morbidity in under five children. Globally, nearly half of under five death are attributable to undernutrition. The number of under-five deaths worldwide was 6.3 million in 2013. About half of under-five deaths occur in only five countries: India, Nigeria, Pakistan, Democratic Republic of the Congo and China. (1) Severe acute malnutrition (SAM) is an advanced state of acute malnutrition which develops when

the body does not get the right amount of vitamins, minerals and other nutrients needed to maintain normal body functions. The prevalence of severe acute malnutrition rate is 3.6 per cent in Pakistan indicating a high rate of malnutrition among children. (2)

The malnourished children especially with severe acute malnutrition (including uncomplicated cases) are highly prone too infections. (3) they many areas in the world with high rates of

childhood malnutrition have little to no diagnostic facility and, in these areas: the most common pathogens infecting malnourished children have barely been characterized on terms of types, prevalence and antibiotic resistance profiles. Moreover the clinical features and basic investigations like complete blood counts cannot suggest the type or site of infection especially in cases of severe acute malnutrition. The use of antibiotics decreases the mortality in severe acute malnutrition. (4-6) the recent recommendation by world health organization (WHO) is to use oral amoxicillin in cases of uncomplicated severe acute malnutrition while injectable benzylpenicillin/ampicillin followed by oral amoxicillin plus gentamycin in cases of complicated severe acute malnutrition. (7) the amoxicillin regimen is not ideal because of its duration (5 days, ten doses) and the potential risks of poor absorption and resistance. (8)

Injectable ceftriaxone seems to be a suitable alternative due to its long duration of action and its sensitivity to bacteria isolated in cases of severe acute malnutrition. (9-10) Dubray C et al (10) 2008 compared daily intramuscular injection with ceftriaxone for 2 days with oral amoxicillin twice daily for 5 days in children aged 6-59 months with severe acute malnutrition and did not find any difference between the case fatality rate of the two groups.

Although WHO has recommended the use of oral amoxicillin as treatment choice in uncomplicated severe acute malnutrition in children but also recommended some parenteral antibiotics (Ceftriaxone IM) in them. The purpose of the study is to compare the efficacy of two days intramuscular ceftriaxone versus five days oral amoxicillin in the treatment of uncomplicated severe acute malnutrition. This study will thus provide the best strategy to adopt to save the lives of uncomplicated acute malnutrition children.

OPERATIONAL DEFINITION

Uncomplicated severe acute malnutrition

The child is said to be suffering from uncomplicated severe acute malnutrition if one is active with good appetite having one or more than one of the following features:

- Weight for length/height less than three standard deviation
- Midarm circumference less than 115mm
- Bilateral pedal edema (defined as bilateral pitting persisting after 3 seconds of thumb pressure on the dorsum of both feet)

Efficacy:

Efficacy of treatment will be labelled as +ve (Yes) if patient survive upto 7 days of hospital stay while on treatment of uncomplicated severe acute malnutrition.

Mortality is defined as the death of patient within 7 days of hospital stay while on treatment uncomplicated severe acute malnutrition. (Patient was followed till 7 days while on treatment of uncomplicated severe acute malnutrition).

MATERIAL AND METHODS

This randomized controlled was conducted at Department of Pediatrics Jinnah Hospital, Lahore from January 2017 to June 2017. Total 70 patients with uncomplicated severe acute malnutrition were selected.

Inclusion criteria:

- Patients with uncomplicated severe acute malnutrition (as per operational definition).
- Patients having age from 6-59 months.
- Both male or female.

Exclusion Criteria:

1. Refusal by the parents/guardians to participate
2. Treatment with any of the study drugs in the 7 days before admission
3. Admission in the last 7 days to any health facility for severe malnutrition
4. Known hypersensitivity to amoxicillin or ceftriaxone
5. On-going vomiting
6. History of convulsion or impaired consciousness in the 24 hours preceding admission

7. No evidence of heart, liver or renal disease

Data collection procedure:

The study was approved by the institution ethical committee. Children with uncomplicated severe acute malnutrition admitting in the ward through emergency or outpatient department fulfilling the inclusion criteria and exclusion criteria were selected. Informed consent was taken from the parents / guardian. Randomization was done by lottery method into group A (Ceftriaxone group) and B (Amoxicillin group). Demographic data as well as brief history and examination was documented on Performa. The nutritional rehabilitation was started according to WHO protocols. The children of group A was given Injection ceftriaxone 50mg/kg intramuscularly daily for two days. The children of group B was given oral amoxicillin in the form of syrup 25 mg/kg per dose twice daily for five days. At day 7, efficacy (Yes/No) of both drugs was noted on pre-designed proforma.

Data analysis:

The collected data was analyzed by SPSS version 10. Mean and SD was calculated for quantitative variables like age. Frequencies and percentages were calculated for qualitative variables like efficacy (Yes/No) and gender for each group. Chi-square test was applied to detect the difference between the efficacies of the both groups. Stratification was done for age and gender. Post stratification chi-square was applied to effect of these on study variable i.e. efficacy. P value \leq 0.05 was considered as statistically significant.

RESULTS

Total 70 children of acute malnutrition were selected for this study. Meant age of the patients was 29.76 ± 16.919 years, mean age of patients of group A was 29.17 ± 17.578 years and group B was 30.34 ± 16.469 years. Efficacy of treatment was noted in 25 (71.43%) patients of group A and in 16 (45.71%) patients of group B. Statistically higher rate of efficacy of treatment was noted in study group A as compared to study group B with p value 0.05. (Table 1).

Stratification in relation to age was done. Out of 18 (51.43%) male patients of group A, efficacy of treatment was noted in 83.33% patients. Total 16 (45.71%) male patients belonged to study group B and efficacy of treatment was noted in 4 (25%) patients. Statistically significant difference of efficacy between the male patients of both groups was noted with p value 0.0014. Total 17 (48.57%) patients of group A and 18 (51.43%) patients of group B were female. Efficacy of treatment was found in 10 (58.82%) and 12 (66.67%) patients of study group A and B respectively. But the difference was insignificant with p value 0.7332. (Table 2)

Patients were divided into four age groups i.e. age group 6-19 months, age group 20-32 months, age group 33-45 months and age group 46-59 months. In age group 6-19 months, out of 13 (37.14%) patients of study group A, efficacy of treatment was noted in 11 (84.62%) patients. Out of 10 (28.57%) patients of study group B, efficacy of treatment was noted in 6 (60%) patients. Statistically insignificant difference of efficacy was noted in both groups with p value 0.3413. In age group 20-32 months, there were 6 (17.14%) patients in group A and 8 (22.86%) patients in group B. treatment was found effective in 4 (66.67%) patients and 4 (50%) patients of study group A and B respectively. But the difference statistically insignificant with p value 0.6270. In age group 33-45 years, out of 10 (28.57%) patients of group A, treatment was found effective in 5 (50%) patients. Out of 11 (31.43%) patients of group B, treatment was found effective in 4 (36.36%) patients. The difference of efficacy between the both groups was statistically insignificant with p value 0.6699. In age group 46-59 years, out of 6 (17.14%) patients, treatment was found effective in 5 (83.33%) patients. Out of 6 (17.14%) patients, treatment was found effective in 2 (33.33%) patients. But the difference of efficacy between the both groups was statistically insignificant with p value 0.2424. (Table 3)

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Table 1: Comparison of frequency of efficacy between the both groups

Group	Efficacy		Total	P value
	Yes (%)	No (%)		
A (ceftriaxone)	25 (71.43)	10 (28.57)	35	0.05
B (amoxicillin)	16 (45.71)	19 (54.29)	35	

Table 2: Comparison of frequency of efficacy between male/female patients

Group	Efficacy		Total	P. Value
	Yes (%)	No (%)		
Male Patient				
A	15 (83.33)	3 (16.67)	18 (51.43)	0.0014
B	4 (25)	12 (75)	16 (45.71)	
Female Patients				
A	10 (58.82)	7 (41.18)	17 (48.57)	0.7332
B	12 (66.67)	6 (33.33)	18 (51.43)	

Table 3: Comparison of frequency of efficacy for age group 6-19 months

Group	Efficacy		Total	P. Value
	Yes (%)	No (%)		
age group 6-19 months				
A	11 (84.62)	2 (15.38)	13 (37.14)	0.3413
B	6 (60)	4 (40)	10 (28.57)	
age group 20-32 months				
A	4 (66.67)	2 (33.33)	6 (17.14)	0.6270
B	4 (50)	4 (50)	8 (22.86)	
age group 33-45 months				
A	5 (50)	5 (50)	10 (28.57)	0.6699
B	4 (36.36)	7 (63.64)	11 (31.43)	
age group 46-59 months				
A	5 (83.33)	1 (16.67)	6 (17.14)	0.2424
B	2 (33.33)	4 (66.67)	6 (17.14)	

DISCUSSION

A high incidence of mortality among children with severe acute malnutrition (SAM) occurs particularly during nutritional crises.(11-12) The care of children with SAM in a therapeutic

feeding centre (TFC) or hospital is based on provision of nutritional rehabilitation and the treatment of associated complications, mainly infections, hypoglycaemia, hypothermia and dehydration.(13) Over the last 20 years, the use of standardised protocols has helped to reduce case

fatality ratios (CFR) among children with SAM.(14-15) In South Africa, an in-hospital CFR decreased from 20% to 6% after the introduction of a standardised nutrition rehabilitation protocol which included an antibiotic regimen of ampicillin and gentamicin.(16)

There is general agreement that administration of systemic broad-spectrum antibiotic therapy on admission improves the outcome of SAM.(17) The World Health Organization recommends that all patients with complicated SAM routinely receive either erythromycin or ampicillin and gentamicin to reduce mortality and improve nutritional response to feeding.(18) However, there is no clear agreement on the most suitable antimicrobial regimen. Amoxicillin has been used routinely in TFCs as first-line antibiotic therapy but little is known about the response and its toxicity in children with SAM. The amoxicillin regimen is not ideal because of its duration (5 days, ten doses) and the potential risks of poor absorption and resistance.(18) Emergence of antibiotic resistance, a factor rarely controlled for in resource-poor settings, might also seriously impair the use of broad-spectrum antibiotics. A hospital study among malnourished children in Kenya described increased resistance to commonly used antibiotics such as erythromycin, ampicillin, cotrimoxazole, chloramphenicol and even oxacillin.(19)

A short course of intramuscular (IM) ceftriaxone might be an alternative to a 5- day regimen of an oral antibiotic. Ceftriaxone has the longest half-life of the cephalosporins. In the treatment of paediatric acute otitis media (AOM), a single IM injection of ceftriaxone 50 mg/kg has been shown to be as efficient as 10-day oral amoxicillin clavulanate at 12.5 mg three times a day.(20) In an urban emergency department (Boston Children's Hospital), two IM injections of ceftriaxone (50 mg/kg) were given to febrile outpatient infants with no source of infection detected on physical examination. It was a successful alternative to hospital admission.(21)

Total 70 children of acute malnutrition were selected for this study. Meant age of the patients was 29.76 ± 16.919 years, mean age of patients of group A was 29.17 ± 17.578 years and group B was 30.34 ± 16.469 years. Efficacy of treatment was noted in 25 (71.43%) patients of group A and in 16 (45.71%) patients of group B. Statistically higher rate of efficacy of treatment was noted in study group A as compared to study group B with p value 0.05.

Dubray C et al (10) 2008 compared daily intramuscular injection with ceftriaxone for 2 days with oral amoxicillin twice daily for 5 days in children aged 6-59 months with severe acute malnutrition and did not find statistically significant difference between the efficacy of both treatment i.e. 70% with amoxicillin and 74.6% with ceftriaxone (P= 0.27). But trehan et al, reported that efficacy was achieved in 39.8% SAM children with amoxicillin. (11)

CONCLUSION

Results of this study showed significantly higher rate of efficacy in patients of acute malnutrition treated with ceftriaxone IV for 2 days as compared to oral amoxicillin for 5 days. Male patients of ceftriaxone group found with higher rate of efficacy as compared to male patients of amoxicillin group but insignificant difference was noted in female patients of both study groups. There was insignificant association between age and efficacy was noted.

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