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ORIGINAL ARTICLE

Efficacy of Oral Azithromycin in Treatment of Uncomplicated Enteric Fever in Children

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ABSTRACT

Background: Enteric fever also known as (typhoid or paratyphoid fever) is a common systemic infection with increased incidence of morbidity and mortality with salmonella typhi and paratyphi. Azithromycin has shown better outcomes in children with uncomplicated disease.

Objective: To determine the efficacy of Azithromycin in treatment of uncomplicated enteric fever in children.

Study Design: Descriptive case series study

Place and Duration of Study: Department of Pediatrics, Sir Ganga Ram Hospital Lahore, Pakistan from 21st August 2015 to 20th February 2016.

Methodology: One hundred and sixty five cases were included. Patients received capsule/suspension of Azithromycin (10 mg/kg/day) OD for 7 days. Treatment was labelled as effective if both clinical and microbiological cure were observed.

Results: Patients ranged between 2-12 years of age. Mean age of the patients was 6.45±2.39 year. There were 85 males (51.5%) and 80 females (48.5%) in this study. Mean duration of fever was 6.97±1.37 days. Clinical cure, microbiological cure and efficacy was 93.9%.

Conclusion: Azithromycin to be effective and safe in treatment of enteric fever. We observed high cure rate of 93.9% without any serious side effects leading to the conclusion that azithromycin is an effective oral agent for treatment for enteric fever.

Keywords: Enteric Fever, Azithromycin, Salmonella Typhi/Paratyphi

INTRODUCTION

Enteric fever is the most common systemic bacterial infection in South Asia. The incidence is about 500 per 100 000.[1-3] Due to rapid rise of resistance against Fluoroquinolones.[4] In salmonella typhi and paratyphoid fever, leading to difficulty in choice of antimicrobial drugs in these diseases.

The emergence of different drug resistance stains in this disease, which is either multidrug resistance or extensively drug resistant typhoid fever, is a consequence of prolonged non-selective usage of antibiotics, which is alarming for Pakistan health services as well as worldwide health authorities. Azithromycin is currently the only oral drug effective against XDR.[5]

Azithromycin or sulphamethoxazole (SXT) have been recommended as first line drugs in the antimicrobial guidelines by the Indian council of medical research, against typhoid fever.[6] These two drugs have been used in many already published literature for typhoid fever.[7,8] Azithromycin was found to be effective againstenteric fever, with minimal resistance currently reported, although concerns persist regarding variations in response to treatment and emerging resistance,[9,10]

MATERIALS AND METHODS

This descriptive case series study in the outpatient department of Sir Ganga Ram Hospital (SGRH) Lahore, Pakistan from 21st August 2015 to 20th February 2016 and 165 patients were enrolled. Informed consent was taken from parents or guardians. On day of recruitment a complete medical, treatment and vaccination history was taken. Complete physical examination was carried out. All patients fulfilling inclusion criteria received capsule/suspension of Azithromycin (10mg/kg/day) OD for 7 days. Children were treated at home and reassessed in Outpatient Department on 7th day after start of treatment in follow-up visit. Temperature pattern history on temperature charting was done on 7th day. First dose of drug was given in hospital. Attendant was informed about follow-up visits. If temperature did notsettle by 4th day of treatment, patient was switched to another antibiotic and was included in treatment failure. All data was collected through pre-designed proforma. For culture 5 ml of venous blood was taken. Blood culture was sent on 7th day. Efficacy was recorded as per operational definition. Study was carried out after taking approval letter from ethical committee of Fatuma Jinnah Medical University/Sir Ganga Ram Hospital, Lahore. Age between 2years to 12 years, both male and females, diagnosed with uncomplicated enteric fever in the last 72 hrs were included. Documented hypersensitivity to Azithromycin (or to any other macrolide), significant underlying heart disease, asthma requiring chronic medications, or immunedeficiencies), documented by previous medical record, those that had treatment with in past 4 days with any antibiotic, Children with poor oral intake were excluded.

Uncomplicated Enteric Fever: fever >38°C of at least 4 days and positive blood culture for Salmonella typhi or paratyphi (>10/HPF). No fluid collection on ultrasound and no air under the diaphragm on X-ray. Clinical cure: Patient becoming asymptomatic (axillary temperature <38°C) within 72 hours of starting treatment and remains afebrile afterwards for at least 48 hours. It was assessed on history taken at 7th day based on temperature checking. Efficacy: Presence of clinical cure and microbiological. Microbiological cure: negative blood culture after 7 days of treatment (no S. typhi/paratyphi per HPF). Data was analyzed using SPSS-20. Drug efficacy was stratified among age, gender and duration of fever to see effect modifier. Chi square test was applied. Post-stratification P-value <0.05 was considered significant

RESULTS

The mean age was 6.45±2.39 years. There were 85 males (51.5%) and 80 females (48.5%). Mean duration of fever was 6.97±1.37 days (Table 1). One hundred and fifty five patients responded to treatment with Azithromycin and their fever settled (<38C) within 72 hrs of starting treatment and remained afebrile for at least 48hrs. Blood cultures of all these patients taken on day 7 were negative (Table 2).

For uncomplicated enteric fever, Azithromycin proved to be efficacious. Clinical cure, microbiological cure and efficacy was 93.9% (Table 3). Stratification with regard to age, gender and duration of fever was carried out and presented (Table 4).

Table 1: Baseline characteristics of trial participants (n=165)

Variable	No.	%
Age (years)		
2-6	88	53.3

7-12	77	46.7
Total	165	100
Gender		
Male	85	51.5
Female	80	48.5
Duration of fever (days)		
5-7	106	64.2
8-9	59	35.8

Table 2: Distribution by types of cure

Variable	No.	%
Clinical cure (axillary temperature <38 for 48hrs)		
Yes	155	93.9
No	10	6.1
Microbiological cure (negative for salmonella typhi/paratyphi)		
Yes	155	93.9
No	10	6.1

Table 3: Efficacy of azithromycin (n=165)

Efficacy	No.	%
Yes	155	93.9
No	10	6.1

Table 3: Comparison of efficacy with respect to age, gender, duration of fever (days)

Variable	Efficacy		χ^2 value	P value
	Yes	No		
Age (years)				
2-6	80	8	3.041	0.081
7-8	75	2		
Gender				
Male	80	5	0.010	0.921
Female	75	5		
Duration of Fever (days)				
5-7	100	6	0.083	0.773
8-9	55	4		

DISCUSSION

In our study, we found high efficacy of oral Azithromycin as a seven-day course of treatment for uncomplicated enteric fever in children. Azithromycin is derived from the basic macrolide nucleus and its action against gram negative bacteria is better as compared to erythromycin. Recent studies on Azithromycin have concluded it to be a safe alternate in treating typhoid fever. Recently, it is also been successfully used against multidrug resistance enteric fever as well. The efficacy of Azithromycin has been proved to be comparable to cephalosporins and fluoroquinolones in many international comparative studies for treating MDR enteric fever.[11-13]

The optimal dosing regimen of Azithromycin for the treatment of enteric fever is not known yet. Most studies use a regimen Dose of 10-20mg/kg/day for seven days are used in many studies.[14] Our study clinical cure rate is 93.9% which is compared with clinical cure rate of previous studies.

Girgis et al[15] and Butler et al[16] found 100% cure rate. Frenck et al[17] found cure rate of 91% which was achieved in 2000 and 94% by Frenck et al[18] in 2004

Oral Azithromycin is an effective treatment option for uncomplicated enteric fever in the outpatient department and used in high-burden countries where fluoroquinolone-resistance is common.[19,20]

Pokharel et al[9] comparedAzithromycin with SXT for 7 days in the treatment of fever of unknown origin including typhoid fever in Nepal. Azithromycin was associated with shorter fever clearance time, fewer treatment failures and fewer adverse events in all patient diarrhea was exceptionally common with Azithromycin.

CONCLUSION

The treating uncomplicated enteric fever Azithromycin at a dose of 100 mg per kg body weight per day for 7 days is effective treatment in adolescents and children. The one dose per day of Azithromycin with the short duration of therapy, better patient compliance and is economical for patients in our setup.

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