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Azithromycin and Ceftriaxone comparison in treating Enteric Fever

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ABSTRACT

Objective: To analyze Azithromycin versus Ceftriaxone as far as interim taken (in number of days) fordefervescence youngsters suffering from enteric fever.

Place and Duration of Study: This observation was taken place at the Department of Paediatrics, Samnabad, Lahore from the month of August, 2018 up till Feburary, 2019.

Materials and Methods: An aggregate of 200 patients were chosen and separated into Group Aand Group B by lottery strategy. Non probability consecutive sampling technique was implemented.All of the patients in Group A were given dosage of oral azithromycin suspension/case (10mg/kg/day; most extreme portion, 500mg/day) once each day fora week and Group B with Intravenous (I/V) Ceftriaxone (75mg/kg/day; greatest place portion, 2.5 g/day) twice a day for 10 days. All drugs were controlled in the medical clinic by nursing staff. The Clinical reaction to the treatment of the two medications was determined as far as number of days taken for defervescence. Information were recorded in-predesignedpro-forma by specialist.

Results: Sex-distribution among the gatherings was irrelevant with p value=0.243.The general mean age of the patients was 4.21 ± 1.22 years. Defervescence savvy conveyance demonstrates that Group A have normal defervescence of 4.53 ± 1.57 days while in Group B it was 4.24 ± 1.22 days which was insignificant with p value = 0.728.

Conclusion: Mean defervescence time of azithromycin is superior to ceftriaxone in the treatment of enteric fever.

Keywords: Enteric fever, Azithromycin, Ceftriaxone.

Introduction

Typhoid fever enteric bacterial disease brought about by Salmonella Typhi and Salmonella Paratyphi; is a typical and wide spread lethal contamination caused in underdeveloped nations particularly in south Asia in light of poor sanitation and poorly treatedwater. It is transmitted by fecal oral course and assessed in excess of 22 million cases worldwide with 200,000 passings consistently have been reported.

Chloramphenicol, Ampicillin, Sulfamethoxazole–Trimethoprim andTetracycline have been generally utilized in the treatment of Typhoid fever. After the obstruction of chloramphenicol in 1970s, Quinolones were begun as1st line treatment of typhoid fever in 1990s.2 Because of the broad use of Quinolones, their defenselessness has diminished causing certain strains becoming impervious to them. Ceftriaxone; a third era cephalosporin, is a exceptionally compelling medication and among the most normally sedate utilized for the treatment of uncomplicated and multi tranquilize safe typhoid fever. 4 Because of parenteral course of organization and delayed defervescence time; Ceftriaxone is not exactly perfect treatment option to Quinolones. Moreover, resistance is likewise creating to these Cephalosporins. Azithromycin; first tested in 1990s with great outcomes is exceptionally encouraging option to Quinolones and Cephalosporins with great fix rates, oral course of organization and aversion of fecal carriage and backslide. It additionally has diminished clinical disappointment, length of medical clinic remain and furthermore very much endured orally when contrasted with others.Clinical reaction was contemplated in one examination where Mean time to defervescence was 4.5 ± 1.9 days for patients who got Azithromycin and 3.6 ± for patients who got Ceftriaxone. Clinical fix by day 7 was 94% in patients who gotten Azithromycin and 97% who got Ceftriaxone.Cost and consistence, just as security and viability, should be viewed as while picking regimens for treating enteric fever in nations with constrained assets where the illness is endemic.Besides, there is no nearby information of Azithromycin adequacy versus Ceftriaxone, there is no examination information accessible after 2004 to think about their Viability and Ceftriaxone is as yet utilized as first line sedate in outdoor patients. We need to analyze both the medications with the goal that better one could be prescribed in future.

Materials and Methods

The study has been approved from hospital ethical committee. Eligible patients were enrolled in trial after taking informed consent. All patients fulfilling the inclusion criteria were included in the study and were admitted in the Inpatient department. 200 patients were divided into Group A and Group B

by lottery method. All patients in Group A were treated with oral azithromycin suspension/capsule (10mg/kg/day; maximum dose, 500mg/day) were administered once daily for 7 days and Group B with Intravenous (I/V)ceftriaxone (75mg/kg/day; maximum dose, 2.5 g/day) were administered twice daily for 10 days. All medications were administered in the hospital by the nursing staff. The Clinical response to the therapy of both drugs were calculated in terms of number of days taken for defervescence. However ifpatient is not improved with above medicines, he was managed with suitable alternate medicines till his/her complete recovery, the drug was labeled non effective and the patient were excluded from the study. Data were recorded in predesigned proforma by researcher. Data were entered and analyzed in SPSS version 17. Frequency and percentages were calculated for qualitative variables like gender of patients. Mean and standard deviation was calculated for quantitative variables like age, time of defervescence (days). Independent samples t-test was used to compare time of defervescence (days) in both the groups with $p<0.05$ as significance level.

Results

200 patients with age range of 3 to 12 years, suffering from enteric fever, were selected and distributed in two groups; group A and group B. In group A, oral azithromycin suspension was administered as 10mg/kg/day, whereas intravenous ceftriaxone was administered in group B as 75mg/kg/day for 7 and 10 days respectively. The Table 1 shows gender distribution among the groups. There were 72 (72%) males and 28 (28%) females in group A, whereas, group B had 59 (59%) males and 41 (41%) females.

Table 1: Gender distribution

Gender	Groups		Total	p-value
	Group A	Group B		
Male	72 (72%)	59 (59%)	131 (65.5%)	0.243
Female	28 (28%)	41 (41%)	69 (34.5%)	
Total	100	100	200	

The mean age for group A was 4.34 ± 1.32, whereas, group B had mean age of 4.11 ± 1.11. Overall mean age was 4.21 ± 1.22. The age distribution had insignificant p value of 0.826. Table 2 shows defervescence and weight wise distribution among the groups. The mean value for defervescence was 4.53 ± 1.57 days for group A and 4.24 ± 1.22 days for group B. The p value was insignificant with value of 0.728.The mean value for weight was 14.63 ± 6.38 for group A and 14.33 ± 6.36 for group B with insignificant p value of 0.637.

Table 2: Defervesence and weight

Variable	Groups	Number of patients	Mean	Standard deviation	p value
Defervesence (days)	Group A Group B	100 100	4.53 4.24	1.5726473 1.226536	0.728
Weight (Kg)	Group A Group B	100 100	14.63 14.33	6.386445 6.364636	0.637

Discussion

Enteric fever is a potentially fatal multisystem illness caused by Salmonella typhi or Salmonella paratyphi. It occurs worldwide where water supply andsanitation are substandard. Enteric fever is highly endemic in developing countries, especially in Asia and Africa, with documented high prevalence among children. It is estimated that more than 26.9 million enteric fever cases occur annually, of which 1% results in death. Azithromycin was tested in the 1990s, with good results, and can now be regarded as a promising alternative to fluoroquinolones and cephalosporins. Nine prospective clinical trials employing azithromycin that enrolled culture-positive children and adults with typhoid fever were carried out inEgypt, India, Vietnam, and Bangladesh.The drug was received by a total of 453 patients, of whom 268 (59%) were children. Its dosage was 10 or 20mg/kg/day for children and 500 mg/day or 1 g/day for adults, given orally for7 days in seven trials and for 5 days in two trials. Two trials were notComparative., 20whereas randomized assignments were made to different comparator drugs in the remaining trials: chloramphenicol in one16 , Ciprofloxacin in one14, ofloxacin in two18,19 , Gatifloxacinin one17, and ceftriaxone in two. Clinical responses in non-comparative trials were that61 of 64 patients (95%) treated with azithromycin were a febrile within 7 days of therapy and were considered to be cured. 15,20 Our study demonstrated that azithromycin is highly effective for the treatment of uncomplicated enteric fever in children. In this study, clinical cure was obtained in 98% of patients treated with azithromycin, whereas in Ceftriaxone group, it was 86%. These findings were comparable with studies

done by Wallace et al.23 and Girgis et al.24 A study by Tribble et al. demonstrated that a 5-day course of azithromycin (20mg/kg per day, with a maximum dose of 1000 mg/day) is effective against uncomplicated enteric fever in children and adolescents.25 In our study, we used a low dose of azithromycin (10 mg/kg/day once a day) for 7 days and tried to compare with ceftriaxone (75mg/kg/day; maximum dose, 2.5 g/day)twice daily for 10 days. One of the reasons for this is to reduce the possible side effects related to the azithromycin usage. Ceftriaxone is highly effective in the treatment of enteric fever but it is less than an ideal drug for its treatment. It shows a slow response with a mean time of 5-7 days or even longer to defervescence, which could be attributed to poor penetration capability of the drug into the cells, and thus difficult to eradicate the bacteria from the intracellular niche. Extended spectrum betalactamase (CTX-M-15 and SHV-12 ESBLs) and CMY2-AmpC beta-lactamase producing S. typhi have been reported. On the other hand, azithromycinpossesses many characteristics for effective and convenient treatment of enteric fever in children with efficacy rate of more than 95%. However, treatment failure rates of 9.3% have been observed in earlier studies. Two other studies have reported a clinical cure rate of only 82% and 92%. In this study we also found that most of the in vitro azithromycin resistant cases responded clinically. Outcomes of treatment were based on duration of defervescence, and development of complications. Regarding duration of defervescence, the average time of defervescence was 4.44 ± 1.25 days inazithromycin group. One previous study104 showed the days of defervescence of azithromycin treatment 4.1 ± 1.1 days. Study by Giris et al 33 found that the days of defervescence with azithromycin treatment was 3.8 ± 1.1 days. Response to treatment with azithromycin was excellent. Franck et al 31 found the cure rate 91% with azithromycin. They concluded that oral azithromycin administered once daily appeared to be effective for the treatment of uncomplicated typhoid fever in children and recommended that the agent could be a convenient alternative for the treatment of typhoid fever, especially in developing countries where medical resources are scarce. Once-daily oral treatment for 7 days (20 mg/kg/day) is convenient and should be favorable for-out-patient compliance. Although parenteral azithromycin is available, it has not yet been popular in typhoid fever treatment. Another study showed that Patients treated with ceftriaxone had a slightly shorter time to defervescence than did those treated with azithromycin (3.9 vs.4.1 days, respectively); however, the difference was not significant, and both results were within time frames reported in previous typhoid treatment trials93.34-37 Mild and transient gastrointestinal symptoms occurred in both treatment groups, but no adverse event was severe enough to require alteration in therapy.

Conclusion

Taking everything into account, azithromycin allowed for 7 days at a measurements of 10 mg/kg/day(maximum portion, 500 mg/day) gives off an impression of being exceptionally viable for the treatment of uncomplicated typhoid fever in kids, with clinical fix rates comparable to those for ceftriaxone. Oncedaily organization of oralazithromycin may offer a basic treatment routine for typhoid fever causedby either vulnerable or sedate safe strains of S. typhi and might be suitable for use in territories where medicinal assets are constrained.

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