ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Feb. 2008, p. 802–803 Vol. 52, No. 2
0066-4804/08/$08.00+0 doi:10.1128/AAC.00867-07

In Vitro Activity of Cefpodoxime, an Expanded-Spectrum Cephalosporin, against *Salmonella enterica* Serotype Typhi[▽]

Antimicrobial therapy is the mainstay for the treatment of typhoid fever. In 1948, Woodward et al. successfully used chloramphenicol to treat patients who had typhoid fever (8). After this accomplishment, the first choice therapy for typhoid fever was chloramphenicol, until the 1970s when the first outbreaks of infection by antibiotic-resistant bacteria appeared (5). There has been an increase in the resistance of strains of *Salmonella enterica* serotype Typhi to chloramphenicol as well as to other drugs, like ampicillin and trimethoprim-sulfamethoxazole, and this emerging multiple drug resistance (MDR) is a major problem in the control of typhoid fever (6, 7). Fluoroquinolones have been proven to be effective for the treatment of typhoid fever caused by MDR strains (1). Recently, reports of patients for whom fluoroquinolone treatment has clinically failed have become the subject of worldwide attention. Due to the emergence of MDR *Salmonella* serotype Typhi in countries where typhoid fever is endemic, the search for alternative antibiotics for treatment is required.

Expanded-spectrum cephalosporins such as cefpodoxime proxetil, ceftriaxone, and cefixime have shown promise as therapies for the treatment of pediatric typhoid (2, 3). However, only cefixime and cefpodoxime proxetil allow oral administration, while ceftriaxone is administered parenterally, for use in ambulatory patients. Also, cefpodoxime proxetil has a favorable pharmacokinetic profile, which allows twice-daily administration.

A representative collection of 90 *Salmonella* serotype Typhi strains were analyzed in this study. These strains were isolated during the period 2003 to 2005 from a prospective surveillance conducted for typhoid fever in two urban slums in eastern Kolkata, India. Identification and characterization of organisms were carried out according to conventional procedures (9).

Antimicrobial susceptibility testing was determined following the Kirby and Bauer disk diffusion method, in accordance with the Clinical and Laboratory Standards Institute (formerly National Committee for Clinical Laboratory Standards), using commercially available antimicrobial disks (Difco, Detroit, MI) (4).

All the *Salmonella* serotype Typhi strains were uniformly susceptible to cefpodoxime, ceftriaxone, and cefixime according to the zone size criterion of the manufacturer. A comparison of ceftriaxone and cefixime zone size data, geometric mean and range, is provided in Table 1. It appears that ceftriaxone is the best choice for the treatment of typhoid fever, but as it is a parenterally administered drug, the choice of cefpodoxime or cefixime as an orally administered agent is preferred for the pediatric population. To date, the fluoroquinolones are the agents of choice for the treatment of MDR typhoid fever. However, the role of this agent in the treatment of children is controversial because of concerns about quinolone-induced arthropathy and cartilage damage. In this setting, cefpodoxime delivers the desired characteristics of an antibiotic and may be the treatment of choice for MDR typhoid fever, particularly with children from areas with a high prevalence of MDR typhoid fever. A study from Pakistan reported about 86% efficacy for cefpodoxime in the treatment of typhoid fever. In Bangladesh, where typhoid fever is also endemic, a clinical trial showed cefpodoxime to be highly efficacious in the treatment of typhoid fever, and it was reported that the cost of cefpodoxime is less than that of cefixime. Our in vitro study shows that oral cefpodoxime provides an effective alternative for the treatment of typhoid fever, particularly for children, even in cases of multidrug-resistant *Salmonella* serotype Typhi, because of its excellent activity.

TABLE 1. Comparison of three antimicrobial agents against *Salmonella* serotype Typhi[a]

Antibiotic	Zone size data	
	Geometric mean (mm)	Range (mm)
Cefpodoxime	24.04	8
Cefixime	23.67	9
Ceftriaxone	26.22	10

[a] Comparative zone size data, including geometric means and ranges, are shown for the activity of three antimicrobial agents against 90 isolates of *Salmonella enterica* serotype Typhi.

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▽ Published ahead of print on 26 November 2007.