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Drug resistance in *Salmonella typhi* in North India with special reference to ciprofloxacin

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Sir,

Antimicrobial agents still remain the mainstay in the treatment of enteric fever; however, indiscriminate use of these drugs has led to the emergence of resistance in *Salmonella typhi*. Many reports are available on drug resistance in *S. typhi* from different parts of India,[1] but there is no report available from the eastern part of northern India. There are reports from India that ciprofloxacin has begun to produce delayed clinical responses in enteric fever[2] with gradual increases in MICs of ciprofloxacin[3] and clinically quinolone-resistant typhoid fever.[4] The present study was conducted to investigate the pattern of drug resistance in isolates of *S. typhi* obtained between 1979 and 1998 in the University Hospital of Banaras Hindu University, Varanasi, with special reference to ciprofloxacin. A total of 140 isolates of the bacterium were tested for antimicrobial susceptibility by agar diffusion and 59 isolates, selected randomly, were subjected to MIC determinations of ciprofloxacin by the agar dilution method as recommended by NCCLS (1997).[5] Plasmids from the three ciprofloxacin-resistant isolates were obtained with a Qiagen-QIA prep spin Miniprep Kit and transformation studies were carried out in *Escherichia coli* (DH5α).

The table shows that co-amoxiclav, cefuroxime and ceftriaxone were effective *in vitro* against >85% of the *S. typhi* tested. Over the study period there was a decrease in the rate of isolates resistant to gentamicin from 22.7% to 9%. Resistance to ciprofloxacin and ofloxacin could be observed even before the introduction of these drugs in the late 1980s into clinical practice in Varanasi. Ciprofloxacin-resistant isolates (three) were found only between 1979 and 1989, whereas ofloxacin-resistant isolates persisted throughout the study period. When resistance to chloramphenicol,

Table. Drug resistance pattern of *Salmonella typhi* during 1979–1998

	Period		
Antimicrobial agent	I 1979–1989 $n = 44$	II 1990–1998 $n = 96$	III 1998 $n = 22$
Amoxycillin	20 (45.0)	44 (47.9)	8 (36.4)
Co-amoxiclav	4 (9.0)	12 (12.5)	2 (9.0)
Cephalexin	24 (54.5)	60 (62.5)	10 (45.4)
Cefuroxime	4 (9.0)	12 (12.5)	2 (9.0)
Ceftriaxone	2 (4.5)	2 (2.1)	0.(0.0)
Gentamicin	10 (22.7)	12 (12.5)	2 (9.0)
Amikacin	0	0	0
Netilmicin	0	2 (2.0)	2 (9.0)
Ciprofloxacin	3 (6.8)	0	0
Ofloxacin	6 (13.6)	6 (6.3)	2 (9.0)
Chloramphenicol	22 (50.0)	52 (54.2)	7 (31.8)
Trimethoprim	18 (40.9)	38 (39.0)	2 (9.0)
Tetracycline	28 (63.2)	62 (64.5)	8 (36.4)
Furazolidone	20 (45.4)	24 (25.0)	2 (9.0)

Values in parentheses are percentages.

trimethroprim and tetracycline was assessed, it was found that there was a considerable decline during 1998. This observation may indicate the return of trimethroprim for empirical use in the treatment of typhoid fever. *In vitro* resistance to furazolidone has fallen dramatically from 45.4% in 1978–1989 to 9% during 1998.

We were surprised to find ciprofloxacin resistance (MIC range 7–125 mg/L) in *S. typhi* isolates before the routine prescription of this drug in clinical practice. However, we have no way of knowing whether these were imported isolates. By contrast, no ciprofloxacin-resistant isolates were found after 1990, when this drug was very much in vogue as a treatment for enteric fever. When these three resistant isolates are excluded, the mean MICs were similar up to (0.03873 mg/L) and after (0.04616 mg/L) 1990. Our findings are unlike those reported from South India,[3] where increases in ciprofloxacin MICs for *S. typhi* have been shown.

When efforts were made to transform the plasmids from the three ciprofloxacin-resistant isolates of *S. typhi* to competent *E. coli* (DH5α), the genes encoding quinolone resistance could not be transformed. This confirms that resistance to ciprofloxacin is chromosomal, as is found in other bacteria.

References

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