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Letters to the Editor

Quinolone antimicrobial resistance in some enterobacteria: a 10-year study in a Venezuelan general hospital☆

Sir,

Quinolones were initially used for treatment of infections caused by Gram-negative bacteria because of their considerable activity against those organisms; later they were also used to treat Gram-positive infections. The in vitro antibacterial activity of new quinolones is broader now than the quinolones available 25 years ago [1]. Although the potential treatment spectrum of these new quinolones has moved from the original focus of urinary tract infections and infections with *Pseudomonas* spp. [2], the activity against enterobacteria is still important. Enterobacteriaceae still cause the majority of urinary tract infections [3]. In developing countries such as Venezuela, where socioeconomic conditions do not allow many individuals access to a clean water supply or adequate sewage disposal, UTI and gastroenteritis are very common infections and are often caused by multiply resistant organisms. Quinolones are an important therapeutic tool in the antimicrobial management of these and despite widespread quinolone use, the emergence of resistance in enterobacteria has been generally slow, although significant in some countries [1,4,5].

We conducted an in vitro study to investigate the antimicrobial susceptibility of *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis* and *Enterobacter cloacae* to eight quinolones over a 10-year period (1993–2002). Isolates came from patients in a general hospital in Caracas (José Gregorio Hernández West General Hospital, Venezuela.

A disk diffusion technique (using Müller–Hinton agar and the Kirby–Bauer technique, according to NCCLS recommendations) [6] was used; the quinolones studied were lomefloxacin, fleroxacin, norfloxacin, ofloxacin, ciprofloxacin, levofloxacin, pefloxacin and moxifloxacin. From 1993 to 2002, 5382 isolates were collected from clinical specimens. The isolates comprised 59.35% *E. coli* ($N = 3194$), 21.85% *K. pneumoniae* ($N = 1176$), 9.75% *E. cloacae* ($N = 525$) and 9.05% *P. mirabilis* ($N = 487$).

Of the total *E. coli* collected, the prevalence of resistance to the quinolones tested ranged from 18.00% (lomefloxacin) to 34.80% (moxifloxacin) (Fig. 1a). The range for *K. pneumoniae* was from 7.90% (levofloxacin) to 16.70% (pefloxacin) (Fig. 1b); for *P. mirabilis*, from 9.00% (levofloxacin) to 22.10% (pefloxacin) (Fig. 1c); and for *E. cloacae*, from 16.70% (ciprofloxacin) to 24.10% (moxifloxacin and pefloxacin) (Fig. 1d).

Trends in resistance rates over the study period (1993–2002) for *E. coli*, *K. pneumoniae*, *P. mirabilis* and *E. cloacae* are shown in Fig. 2a–d, respectively.

Around 80% of *E. coli* and *E. cloacae* were susceptible to lomefloxacin and nearly 90% *K. pneumoniae* and *P. mirabilis* to lomefloxacin at the end of the study period.

Ciprofloxacin resistance in *E. coli* (about 25%) was comparable with levofloxacin, ofloxacin, norfloxacin, pefloxacin and fleroxacin (Fig. 2a).

Ciprofloxacin and levofloxacin in *K. pneumoniae*, were both low, around 10% and the resistance prevalence to norfloxacin and lomefloxacin was slightly higher (Fig. 2b).

For *P. mirabilis*, the resistance prevalence to ciprofloxacin, ofloxacin, lomefloxacin and norfloxacin was in the range 15–18%. That of perfloxacin was lower at 10% whereas that of perfloxacin was significantly higher at 27% ($p = 0.0037$) (Fig. 2c).

Ciprofloxacin was still most active against *E. cloacae* at the end of the study period but had similar activity to lomefloxacin, ofloxacin and levofloxacin. It was significantly more active than norfloxacin, pefloxacin and moxifloxacin ($p < 0.05$) (Fig. 2d).

Lomefloxacin, followed by levofloxacin and ciprofloxacin showed the highest overall antimicrobial activity against the organisms evaluated over this study period.

Resistance of *E. coli* to the different quinolone was roughly comparable. Enterotoxigenic *E. coli* has been identified as the cause of traveller's diarrhoea in 16% patients in some studies [7]. However, there is significant resistance in such organisms to ampicillin, tetracycline and trimethoprim-sulphamethoxazole resistance, as also occurs in enteroaggregative *E. coli*, also a cause of traveller's diarrhoea in up to 9% patients [8]. Chloramphenicol and co-trimoxazole showed moderate activity against these organisms and amoxicillin plus clavulanic acid, nalidixic acid and ciprofloxacin showed very good activity.

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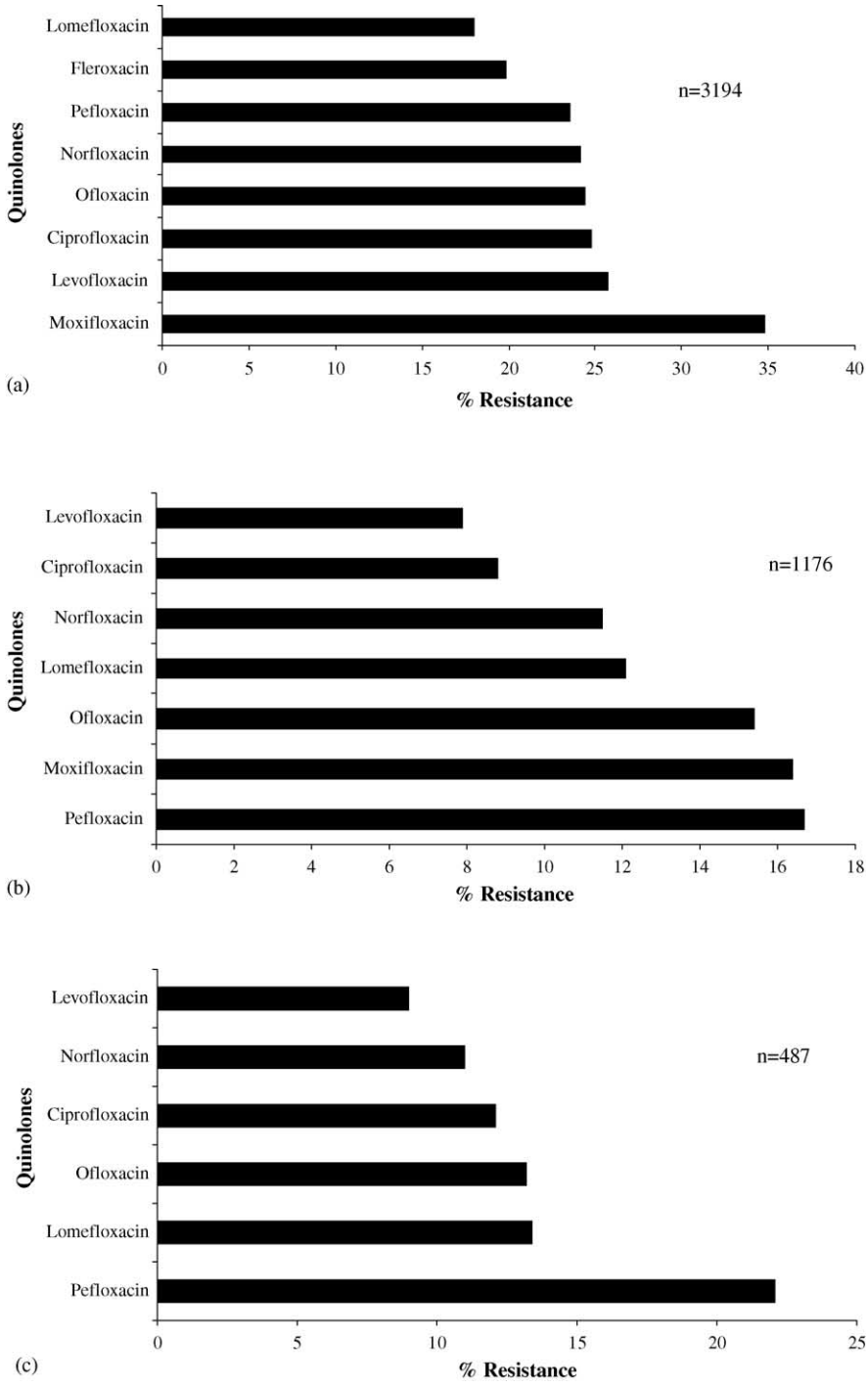

Fig. 1. Total resistance of four species of Enterobacteriaceae collected at the Caracas West General Hospital, Venezuela, 1993–2002, against quinolones. (a) *Escherichia coli*; (b) *Klebsiella pneumoniae*; (c) *Proteus mirabilis*; (d) *Enterobacter cloacae*.

In one study, resistance to nalidixic acid was demonstrated in three isolates, two from patients who had travelled to India [8]. In all three strains, the resistance was linked to mutations in the *gyrA* gene alone or in both *gyrA* and *parC* genes. Ciprofloxacin showed excellent in vitro activity and could be useful in the treatment of travellers' diarrhoea [8].

In Latin America, molecular characterisation of ciprofloxacin-resistant *E. coli* showed that most strains have a double mutation in the *gyrA* gene associated with a single mutation in the *parC* gene [9].

For *K. pneumoniae*, ciprofloxacin showed an excellent antimicrobial activity, comparable with lomefloxacin, norfloxacin and levofloxacin. In published studies, more than