Ciprofloxacin resistance—‘early-warning’ signs from the MYSTIC surveillance programme?

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Sir,

Over the last few decades the ever-increasing level of bacterial resistance to antimicrobial action has been a cause of worldwide concern. The continuous development of new compounds to combat multidrug-resistant strains of bacteria is constantly challenged by the ability of the microbes to develop new mechanisms for defence. This situation is compounded by the indiscriminate and/or inappropriate use of antimicrobial agents. Longitudinal surveillance studies are one of the main tools for tackling the problem of antimicrobial resistance, as they enable resistance patterns to be monitored and allow early detection of any potential resistance trends. In this way the spread of resistance genes may be prevented by revising antimicrobial usage protocols and improving measures to reduce cross-infection. The usefulness of such an ‘early-warning system’ hinges on the rapid dissemination of information to those concerned so that such measures can be initiated as soon as possible. Although it is well recognized that the increased use of ciprofloxacin (CIP) over the last decade has led to a progressive loss of susceptibility, particularly among Gram-negative bacteria, it is worrying that the latest results from the Meropenem Yearly Susceptibility Test Information Collection (MYSTIC) indicate that this trend is not abating.

MYSTIC is a global, year-on-year, antimicrobial surveillance programme that collects data on antimicrobial resistance patterns from centres (intensive care units, neutropenia units, cystic fibrosis units and general wards) where meropenem (MEM) is prescribed. As well as MEM, MICs of imipenem (IPM), ceftazidime (CAZ), gentamicin (GM), piperacillin/tazobactam (TAZ) and CIP are determined, using NCCLS-recommended methodology.

During the period 1997–2000, over 1475 aerobic, distinct, clinical Gram-negative isolates were obtained from a group of UK hospitals. Isolates were speciated by each hospital using standard methods. A total of 1278 (86.7%) of the Gram-negative isolates (45 species) was CIP susceptible and intermediate (using the NCCLS definitions of susceptible (≤1 mg/L), intermediate (2 mg/L) and resistant (≥4 mg/L)). One hundred and ninety-seven (13.4%) Gram-negative strains (22 species) were CIP resistant, of which *Pseudomonas aeruginosa* (n = 67), *Acinetobacter*...
CIP resistance is associated with marked levels of co-resistance to other commonly used antimicrobials in serious infections. Overall, the carbapenems (MEM and IPM) showed the greatest activity against both CIP-susceptible/intermediate (92.4 and 88.4%, respectively) and CIP-resistant (72.1 and 75.1%, respectively) organisms. All the other agents tested demonstrated lower susceptibilities than the carbapenems and, in CIP-resistant compared with CIP-susceptible/intermediate organisms, more marked reductions in susceptibility: GM = 81.8 and 51.8%, respectively; TAZ = 78.8 and 47.2%, respectively; and CAZ = 67.6 and 26.4%, respectively.

Equally as worrying as the marked co-resistance in CIP-resistant isolates is the observation of a possible trend towards a progressive loss of susceptibility to CIP that was seen between 1997 and 2000 in both the CIP-susceptible and CIP-resistant groups (Figure). In contrast, MEM showed no observed reduction in activity against Gram-negative isolates including CIP-resistant strains.

The real significance of these data indicating a trend has yet to be determined and the development of an appropriate statistical test is under way. Precise statistical analysis of the information gathered so far, together with data from the continuation of the MYSTIC programme, will provide a clearer picture. In the meantime, however, it is essential that those concerned be alerted to the possibility of a trend towards further increased resistance to CIP and its co-resistances, so that the judicious use of CIP and its alternatives can be considered. Carbapenems appear to be the least affected, which make them potential first-line alternatives to CIP particularly in areas of high fluoroquinolone resistance rates amongst Gram-negative bacteria.

References