Reviewer’s report

Title: Clinical outcomes in typhoid fever: adverse impact of infection with nalidixic acid-resistant Salmonella typhi

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Reviewer: John Threlfall

Reviewer’s report:

The manuscript provides a comprehensive account of the treatment of 60 patients infected with Salmonella Typhi (S. Typhi) in a tertiary care hospital in north India from 2001 to 2003. It is noteworthy that 11 patients had treatment failure following therapy with fluoroquinolone antibiotics, based on the definition applied. The majority of patients who did not respond satisfactorily to fluoroquinolone therapy were infected with strains resistant to nalidixic acid, with concomitant decreased susceptibility to fluoroquinolones.

The main conclusions from the investigation are as follows:

Resistance to nalidixic acid appeared to increase the severity of illness. Whether this was due to pre-treatment with fluoroquinolones is not clear.

Decreased susceptibility to fluoroquinolones cannot be detected using NCCLS guidelines.

On the basis of these observations the authors have recommended that fluoroquinolones should no longer be used as first-line therapy in populations where nalidixic acid is common in S. Typhi.

Comments

There is no doubt that the authors have conducted a very detailed investigation, which appears to be statistically sound. Regrettably their main finding, that resistance to fluoroquinolones cannot be detected using NCCLS guidelines, is not new and merely reiterates what has been stated by others on numerous occasions. In this respect it is particularly important that the publication by Aarestrup and others (AAC, 2003; 47) should be cited.

The recommendation that fluoroquinolones should no longer be used as first-line therapy in populations where nalidixic acid is common in S. Typhi is very difficult to justify. Although there is no doubt that treatment failures do occur, particularly in relation to duration of fever, etc, there are many reports, which have emphasised that fluoroquinolones, should remain the first-line drug of choice, but that physicians should be aware that treatment failures may occur in some cases. Ciprofloxacin is a relatively cheap drug, and many countries could not afford to use the third-generation cephalosporins for this purpose other than in cases where the patient is not responding to treatment.

Recommendation:

Reject - work is for the most part confirmatory of what has already been published elsewhere.