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Guidelines to Authors
Ciprofloxacin Breakpoints in Enteric Fever - Time to Revise our Susceptibility Criteria

Dear editor,

Apart from its considerable morbidity and absenteeism, enteric fever today consumes vast resources in developing nations. Most laboratories in India follow the Enterobacteriaceae CLSI guidelines for ciprofloxacin with an MIC of ≤1 mg/mL and zone diameter of ≥21 mm being considered as susceptible for Salmonella.

In Mumbai, resistance to nalidixic acid in Salmonella typhi has steadily increased from 0% in 1992 to 82% in 2000 and 86% in 2002.[1,2] However, in vitro susceptibility to ciprofloxacin may be seen on the basis of breakpoints that were established more than a decade ago. Clinical failure and increasing MIC to ciprofloxacin in salmonellae has prompted most clinicians to reconsider its use despite apparent in vitro susceptibility. Yet we need to re-iterate that ciprofloxacin, when susceptible, is still an ideal choice for treatment of enteric fever in the subcontinent.

In an attempt to address this issue, we analysed a total of 96 nalidixic acid-resistant (no zone of inhibition on disc diffusion) blood culture isolates in the year 2005 - 44 of S. typhi and 52 S. paratyphi A (Table).

Two criteria were considered: (1) Keeping the current CLSI (January 2006) recommended guidelines for MIC of Enterobacteriaceae in mind, based on a regression analysis of log MIC vs. zone diameter, to accommodate a susceptible MIC of ≤1 µg/mL, the zone diameter for ‘susceptible’ was increased to ≥27 mm from 21 mm with a corresponding increase in the zone diameter for resistant isolates from ≤15 mm to ≤21 mm for resistant MIC of ≥4 µg/mL. (2) Keeping pharmacokinetic and pharmacodynamic principles for gram-negative bacteria in mind (AUC/MIC >125), with a 750 mg twice daily dose of ciprofloxacin, the attainable AUC is 31.06 µg.h/mL, allowing a maximum MIC of <0.25 µg/mL to be regarded as susceptible.

In our analysis, all the isolates of S. paratyphi A had a MIC ≥1 µg/mL, making ciprofloxacin no longer an option available for therapy for this organism. However, there were 12 S. typhi isolates with an MIC of <0.25 µg/mL, 9 of them with a zone diameter of >30 mm. Thus for a PK/PD breakpoint, we suggest that the MIC of ciprofloxacin be lowered to ≤0.25 µg/mL and the resistant zone diameter breakpoint be increased to ≤28 mm and the susceptible one to ≥30 mm. Either way, we believe that the zone diameters must increase for S. typhi and S. paratyphi A.

References

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Received: 09-02-07
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<th>22-25</th>
<th>26</th>
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<th>≤28</th>
<th>29</th>
<th>30</th>
<th>≥31</th>
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<td>MIC (µg/mL)</td>
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Table: Correlating MIC and zone diameters of enteric fever isolates