Ciprofloxacain Breakpoints in Enteric Fever: Time to Revise our Susceptibility Criteria

Dear Editor,

We read with interest the article entitled “Ciprofloxacain breakpoints in enteric fever-time to revise our susceptibility criteria” by Rodrigues et al.[1] published in Jan-Mar 2008 issue of the Indian Journal of Medical Microbiology. The article is thought provoking but certain critical aspects have been overlooked, which if mentioned would be enriching for the various investigators and decision makers in this crucial area.

Firstly, this study only mentions the number of nalidixic acid resistant strains isolated in 2005, but does not mention the total number of Salmonella typhi isolates from which they have been characterized. This does not allow us to calculate the prevalence of nalidixic acid resistant strains in a geographical area, which in this study happens to be Mumbai. Secondly, the methodology used in obtaining the results has not been mentioned. The MIC values are known to vary significantly with the methodology used.[2] To revise the susceptibility criteria in our country all the centers working on S. typhi should follow same methodology. Thirdly, this study does not comment on the clinical outcome of the cases from which the 96 nalidixic acid resistant strains have been isolated. The increased MIC values of ciprofloxacain in S. typhi in India have been reported since many years,[3,4] but the important issue that has not been adequately addressed in many of these studies is the extent of clinical failure. Fourthly, this article mentions that the attainable AUC of ciprofloxacain is 31.06 μg/mL with 750 mg twice daily dose of ciprofloxacain, which is a satisfactory PK-PD value for the treatment of S. typhi enteric fever. However, there is evidence to suggest that free drug AUC and not the total AUC is more predictive of clinical success. [2] Considering plasma protein binding of approximately 30% for ciprofloxacain, for 750 mg b.d. daily dose, AUCfree gets reduced to 22, and at MIC = 0.25μg/mL, AUCfree:MIC ratio becomes 88.[5] This implies a dose of 750 mg b.d. daily would also be inadequate, as the recommended AUCfree:MIC ratio for gram negative microorganisms is >100.

References


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Received: 26-03-08
Accepted: 03-05-08