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Gatifloxacin

A Viewpoint by Helen Giamarellou

4th Department of Internal Medicine, Athens Medical School, Sismanoglio General Hospital, Athens, Greece

Gatifloxacin, a new 8-methoxy fluoroquinolone with a 3-methylpiperazinyl substituent at C7, belongs to the so-called "broad spectrum quinolones" in the group which also includes trovafloxacin, sparfloxacin, levofloxacin, lomefloxacin, grepafloxacin, moxifloxacin, clinafloxacin, sitafloxacin and gemifloxacin. In common with the "classic quinolones", i.e. ciprofloxacin, ofloxacin and pefloxacin, they have anti-enterobacteriacidal activity, but are characterised by their strengthened potential against Gram-positive cocci, including penicillin-resistant pneumococci and enterococci as well as several methicillin-resistant *Staphylococcus aureus* strains.

Gatifloxacin, when compared with the standard quinolone ciprofloxacin, exhibited ≤2 fold activity against Enterobacteriaceae and showed less activity against *Pseudomonas* spp. However, along with trovafloxacin, gatifloxacin is very potent against *Acinetobacter* spp. and *Stenotrophomonas maltophilia* strains, and in common with moxifloxacin and trovafloxacin it possesses promising activity against anaerobes including *Bacteroides fragilis* strains.[1]

Using a susceptibility breakpoint of ≤2 mg/L, gatifloxacin at 0.5 mg/L killed 90% of penicillin-resistant and penicillin-intermediate pneumonococci as well as viridans and β-haemolytic streptococci. Although the parenteral management of pneumococcal pneumonia with benzylpenicillin does not appear to be influenced by the levels of penicillin resistance currently encountered,[2] as gatifloxacin also possesses excellent *in vitro* activity against other major respiratory pathogens it will become an attractive compound in the treatment of community-acquired respiratory tract infections. Indeed, from therapeutic trials of gatifloxacin conducted in North America and Japan currently reported only as abstracts, clinical cure rates with a single daily oral dose of 400mg were ≥89% in cases of acute exacerbations of chronic bronchitis and community-acquired pneumonia, including both pneumococcal and atypical pneumonia cases.

It should be pointed out, however, that recently among Canadian strains of *Streptococcus pneumonia* resistant to ciprofloxacin (MIC ≥4 mg/L), only 63, 64, 68, 77, 75 and 88% were susceptible to the breakpoint (2 mg/L) of levofloxacin, sparfloxacin, grepafloxacin, trovafloxacin, gatifloxacin and moxifloxacin, respectively.[3] Unfortunately, reduced susceptibility to the new quinolones has been associated with resistance to penicillin, and the reported Canadian data led the authors to suggest that the increased prevalence of resistance in pneumococci was due to selective pressure resulting from the increased use of fluoroquinolones in retail pharmacies.

Gatifloxacin has a broad antibacterial spectrum, advantageous kinetic properties (elimination half-life ≈ 8 hours, negligible metabolism, >80% renal elimination, low protein binding and promising lung, bone and skin tissue penetration) permitting once-daily administration. Gatifloxacin also has the lowest potency among several newer quinolones on hepatic microsomes, thereby minimising its interaction potential. In addition, it has a good tolerability profile (with the exception of minor gastrointestinal tract disturbances in ≤8% of patients) without reports of phototoxicity, crystalluria or tendinitis. Thus, there is no doubt that gatifloxacin will also be prescribed for the treatment of complicated urinary tract infections, chronic prostatitis and skin and soft tissue infections as well as in surgical infections. However, serious consideration should be given to the fact that if the value of this important newer quinolone is to be preserved, it is essential for the physician to control its inappropriate use in the community. ▲

References

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