plasmid TPqnrS-1a do not share any obvious structural similarities. A comparison between the TPqnrS-1a-associated QnrS1 protein and the 218-amino-acid proteins from Vibrio splendidus (accession no. EAP95542) and Vibrio spp. (accession no. EAQ55748)—the latter two considered as a natural reservoir of qnrS genes—revealed 83% and 82% amino acid identity, respectively, and 91% amino acid similarity.

Previous studies revealed that the qnrS1 gene is often located on large plasmids that carry additional resistance genes. Although plasmids pAH0376 from S. flexneri and pINF5 from Salmonella Infantis carried a complete Tn3 with a bla_{TEM-1} β-lactamase gene, recently discovered plasmids of E. cloacae identified the qnrS1 gene in close proximity to the novel β-lactamase gene bla_{LAP-1}. In the present study, we characterized a comparatively small plasmid that carried the qnrS1 gene as the sole resistance gene. To the best of our knowledge, plasmid TPqnrS-1a is the first qnrS1-carrying plasmid for which the complete sequence is available. A detailed sequence analysis of this plasmid suggested that it has most likely derived from an interplasmid recombination event between a qnrS1-carrying plasmid such as pINF5 from Salmonella Infantis or pS5-1 from E. cloacae and a small mobilizable plasmid similar to pEC278 from E. coli. The identification of qnrS1 genes on structurally diverse plasmids points towards the dissemination of these genes and their adaptation in new hosts as relevant factors in the emergence of transferable quinolone resistance.

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Transparency declarations

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References


Activity of iclaprim against Legionella pneumophila

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Sir, Legionella pneumophila is an ‘atypical’ pathogen associated with lower respiratory tract infections (RTIs) such as community-acquired pneumonia (CAP). Organizations such as the Infectious Diseases Society of America recommend that empirical treatment of CAP should cover atypical pathogens such as L. pneumophila and Chlamydia pneumoniae. At present, macrolides and fluoroquinolones are the most active options against atypical pathogens. On the contrary, β-lactams are inactive against these pathogens.

Iclaprim is a new dihydrofolate reductase inhibitor, which recently completed enrolment in two Phase III trials of complicated skin and skin structure infections treated via intravenous administration and has recently successfully completed Phase I investigations of an oral formulation. Currently, the only clinically available antibiotic targeting dihydrofolate reductase is trimethoprim. This antibiotic can be used in combination with sulphonamides such as sulfamethoxazole, although rarely these days due to concerns over toxicity with sulfamethoxazole. At present, data on the activity of iclaprim against L. pneumophila have not been published.

Iclaprim (Arpida AG, Reinach, Switzerland), trimethoprim, sulfamethoxazole, trimethoprim/sulfamethoxazole (19:1 ratio), clarithromycin and levofloxacin (all from Sigma, Poole, UK) were investigated against 56 L. pneumophila isolates. The isolates were derived mostly from clinical material examined in hospitals or reference centres worldwide. MICs were determined using an agar dilution method. The agar consisted of 1% yeast extract (Oxoid Ltd, Basingstoke, UK), 1.3% Bacteriological Agar No. 1 (Oxoid), 5% water-lysed horse blood (Oxoid) and legionella growth supplement (Oxoid). The inoculum used was ∼10^5 CFU of each isolate contained in a volume of 1 μL. After 48–72 h of incubation in air at 35°C, MIC was determined as the lowest concentration of antimicrobial tested that inhibited growth of the inoculum, disregarding a single persisting colony or a faint haze caused by inoculation.

Summary MIC data are presented in Table 1. Iclaprim was very active, with 16-fold lower MIC_{50} or MIC_{90} values than...
trimethoprim alone. Sulfamethoxazole was essentially inactive and the combination of trimethoprim and sulfamethoxazole was also less active than iclaprim, despite showing a 4-fold synergy when compared with trimethoprim alone. Iclaprim had activity similar to that observed with clarithromycin, but was less active than levofloxacin.

These data show that iclaprim has promising in vitro activity against L. pneumophila. These results, in combination with its high concentration in alveolar macrophages and epithelial lining fluid, oral bioavailability and activity against other RTI pathogens such as Streptococcus pneumoniae, Haemophilus influenzae, Streptococcus pyogenes and C. pneumoniae, make iclaprim a potentially useful new agent for the treatment of RTIs.

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