Sub-inhibitory concentrations of vancomycin prevent quinolone-resistance in a penicillin-resistant isolate of Streptococcus pneumoniae

ABSTRACT

Considering the risk of quinolone-resistance in pneumococci, the observation might be of clinical importance.

INTRODUCTION

Background Since the late seventies, the worldwide emergence of penicillin-resistant pneumococci has jeopardized the efficacy of β-lactam antibiotics, in life threatening infections such as meningitis or pneumonia. Moreover, penicillin-resistant pneumococci are often resistant to multiple other drugs, thus restricting the choice of alternative compounds. Therefore, new anti-pneumococcal drugs should combine the abilities to (i) rapidly inhibit and kill the target organisms, (ii) penetrate in various body compartments, including the cerebrospinal fluid, and (iii) impede resistance development against the new compounds. Newer quinolones with good anti gram-positive activity, including trovafloxacin, might fulfill these criteria. However, quinolone-resistant pneumococci can arise by acquisition of only one or two mutations in the genes of the quinolone targets, i.e., the topoisomerase IV (parC and parE) and the gyrase (gyrA and gyrE) [,]. This mechanism of resistance is much less complicated than acquisition of resistance to penicillin by transformation with major gene sequences for PBPs. One would therefore expect that the activity of quinolones against pneumococci is already jeopardized. Indeed, recent data support this notion. Recently, we observed that addition of vancomycin to trovafloxacin improved the bactericidal activity of the quinolone against penicillin-resistant pneumococci both in vitro and in rabbits with experimental meningitis. We now demonstrate that sub-inhibitory concentrations of vancomycin (¼ MIC: 0.03 mg/L), that did not affect the quinolone MIC per se, also drastically prevented resistance to ciprofloxacin, and totally prevented resistance to trovafloxacin. The observation deserves attention because it might be of clinical relevance.

CONCLUSION

Conclusions The data observed here are reminiscent of the synergic activity of cell wall active antibiotics and aminoglycosides in enterococci and other gram-positive pathogens. Although the mechanism of this synergism is not entirely clear, it is important both to prevent resistance and improve therapeutic efficacy in severe infections. A similar model could hold true with the combination of cell wall inhibitors and trovafloxacin or other quinolones in pneumococcal infections. Therefore, the present observation with vancomycin and quinolones might be of clinical relevance both for resistance prevention and treatment efficacy. Moreover, it opens the avenue to other drug combinations.