GidB mutation as a phylogenetic marker for Q1 cluster *Mycobacterium tuberculosis* isolates and intermediate-level streptomycin resistance determinant in Lisbon, Portugal

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Abstract

Development of streptomycin resistance in *Mycobacterium tuberculosis* is usually associated with mutations in *rpsL* and *rrs* genes, although up to 50% of clinical streptomycin-resistant isolates may present no mutation in either of these genes. In the present report we investigate the role of gidB gene mutations in streptomycin resistance. We have analyzed 52 streptomycin-resistant and 30 streptomycin-susceptible *Mycobacterium tuberculosis* clinical isolates by sequencing and endonuclease analysis of the *gidB* and *rpsL* genes. All clinical isolates were genotyped by 12-loci MIRU-VNTR. The *gidB* gene of 18 streptomycin-resistant isolates was sequenced and four missense mutations were found: F12L (1/18), L16R (18/18), A80P (4/18) and S100F (18/18). The remaining isolates were screened by endonuclease analysis for mutations A80P in the *gidB* gene and K43R in the *rpsL* gene. Overall, mutation A80P in the *gidB* gene was found in eight streptomycin-resistant isolates and 11 streptomycin-susceptible multidrug-resistant isolates. Also noteworthy, is the fact that *gidB* mutations were only present in isolates without *rpsL* and *rrs* mutations, all from genetic cluster Q1. Streptomycin quantitative drug susceptibility testing showed that isolates carrying the gidB A80P mutation were streptomycin intermediate-level resistant and that standard drug susceptibility testing yielded inconsistent results, probably due to borderline resistance. We conclude that *gidB* mutations may explain the high number of streptomycin-resistant strains with no mutation in *rpsL* or *rrs*. These mutations might occasionally confer low-level streptomycin resistance that will go undetected in standard susceptibility testing.

Intravenous antibiotics given for 2 weeks do not eradicate persistent *Staphylococcus aureus* clones in cystic fibrosis patients

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Abstract

Staphylococcus aureus is the most commonly isolated pathogen in respiratory tract secretions from young patients with cystic fibrosis (CF), and several treatment strategies are used to control the infection. However, it is not known whether intensified treatment with antimicrobial agents causes eradication of S. aureus clones. We retrospectively determined the impact of intravenous (IV) antimicrobial agents on the suppression and eradication of S. aureus clones. One thousand and sixty-one S. aureus isolates cultured from 2526 samples from 130 CF patients during a 2-year study period were subjected to spa typing. Intervals between positive samples and the occurrence of clone replacements were calculated in relation to courses of IV antimicrobial agents. Of 65 patients chronically infected with S. aureus, 37 received 139 courses of IV antimicrobial agents with activity against S. aureus (mean duration, 15 days; range, 6–31 days). Administration of IV antibiotics increased the time to the next sample with growth of S. aureus: the mean interval between two positive samples was 68 days if IV treatment had been administered, in contrast to 49 days if no IV treatment had been administered (p < 0.003). When S. aureus recurred in sputum after IV treatment, the isolate belonged to a different clone in 33 of 114 (29%) intervals, in comparison with 68 of 232 (29%) intervals where IV treatment had not been prescribed (OR 0.98, 95% CI 0.60–1.61). In conclusion, we show that 2 weeks of IV antimicrobial treatment can significantly suppress chronic staphylococcal infection in CF, but is not associated with the eradication of persistent bacterial clones.