

Sequence analysis of the *embB* gene for identification of mutations associated with resistance of multidrug-resistant *Mycobacterium tuberculosis* strains to ethambutol

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Background

Ethambutol (EMB) is a first-line drug for the treatment of tuberculosis that targets the cell wall of tubercle bacilli through interfering with arabinosyl transferases, encoded by the *embAB* genes and involved in the biosynthesis of arabinogalactan and lipoarabinomannan, the key structural components of the mycobacterial cell wall. Mutations in the *embB* gene, and those within its conserved EMB resistance determining region (ERDR) in particular, have been associated with resistance to EMB in *Mycobacterium tuberculosis*. Analysis of mutations in the *embB* gene in *M. tuberculosis* strains may contribute to the development of new tests for rapid detection of EMB resistance.

Objective

The aim of this study was to examine the mutational “hot spots” in the *embB* gene, including the ERDR, among multidrug-resistant (MDR) *M. tuberculosis* clinical isolates and to find a possible association between *embB* mutations and resistance to EMB.

Methods

A 863-bp region of the *embB* gene of 48 clinical isolates of *M. tuberculosis* (21 EMB-resistant, 27 EMB-susceptible), recovered from as many MDR-TB patients in Poland in 2004 was sequenced and screened for mutations linked to EMB resistance. Mutations in the *embB* gene were detected by comparing DNA sequences with the corresponding sequences of a wild-type reference laboratory strain *M. tuberculosis* H37Rv. The obtained results were interpreted in the context of EMB susceptibility profile of the strains tested.

Conclusions

In total, 7 *embB* mutation types were detected in 6 distinct codons of 26 (54.2%) *M. tuberculosis* strains tested. Only 10 of those strains were EMB-resistant and had mutations either in codon 306 (7 strains) or 406 (3 strains). None of the two mutation types were found exclusively in EMB-resistant strains. Analysis of other genetic loci is needed for the identification of more specific mutations associated with EMB resistance.

Keywords:

Mycobacterium tuberculosis; *embB*; ethambutol; multidrug-resistance; sequence analysis