Ethambutol-resistance testing by mutation detection using MTBDRsl

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ABSTRACT

Aims and objectives: Despite the successes in managing drug-susceptible TB, drug-resistant (DR) tuberculosis is a major challenge to the effectiveness of National Tuberculosis Program in Armenia, placing the country in the list of 18 high-burden countries for MDR-TB in the WHO European Region. Estimated burden of MDR-TB in 2012 was 9.4 (7–12) and 43 (38–49) among retreatment TB cases. A total of 92 laboratory confirmed cases had been reported to the WHO (57 new and 35 previously treated) out of 511 cases tested for MDR-TB. GenoType MTBDR plus is a new molecular kit designed for rapid identification of the resistance to the second-line antituberculosis drugs with a single strip. The aim of this study was to identify the mutation that confers resistance to ethambutol (EMB) in Mycobacterium tuberculosis in comparison with the phenotypic drug susceptibility test (DST). Ethambutol is used in M/XDR-TB regimens only if it is susceptible by DST results.

Methods: A set of 173 drug resistances TB isolates during 2011 and 2012 period, being either acid fast bacterium positive or negative but culture positive resistant to isoniazid, rifampin, or both according to the GenoType MTBDR plus assay were consecutively tested, using the GenoType MTBDRsl (MTBDR plus version 1.0 and MTBDRsl version 2.0 Hain Lifescience, Nehren). embB gene analysis and the results were compared to phenotypic EMB testing (DST). The DNA preparation method used as described recommended by the manufacturer.

Results: Genotypic analysis identified mutations at codon 306 of the embB gene in 20.8% (36/173) and miss band of wild type in 12.71% (22/173) of the resistant isolates in comparison to only 14.45% (25/173) of those that were phenotypically resistant to EMB by DST MGIT liquid media. Mutation locus were identified in embB MUT1B and embB MUT1A 8.67% (15/173) and 12.13% (21/173), simultaneously.

Phenotypic retesting in MGIT demonstrated that 45 (306 of the embB gene and miss band of wild type together) genotypically resistant isolates were phenotypically resistant to EMB. This implies that 58.62% (33/58) of EMB resistance had been phenotypically missed by routine laboratory procedures. EMB resistance was closely linked to multidrug resistance (MDR); 70.69% (41/58) of the EMB-resistant isolates were resistant to both isoniazid and rifampicin.

Conclusion: Implementation of more accurate diagnosis of EMB resistance may enhance patient management in Armenia, as standardized treatment of MDR-TB with second-line drugs is currently dependent on the outcome of the EMB resistance test.

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