The Molecular ‘MDR Screen’ is an Important Tool in the Diagnosis and Initiation of Appropriate Therapy in TB Patients in the State of Florida

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Abstract

Objective: The Florida Department of Health Bureau of Public Health Laboratories (BPHL) algorithm for the diagnosis and anti-mycobacterial susceptibility testing (AST) of tuberculosis (TB) includes a molecular MDR (multi-drug resistance) screen for the rapid and accurate detection of drug resistance in TB. This study reviews the performance of the MDR screen and initiation of appropriate TB patient therapy.

Study Design: Analysis of all AST data over a 2-year period was performed, followed by review of treatment records for MDR-TB patients. The following was determined: date of MDR screen result for Hain Genotype MTBDRplus assay, version 2 (Hain LifeScience); date of phenotypic AST result by Sensititre MIC assay (TRIK Diagnostic Systems, Thermo Fisher); and date of initiation of appropriate MDR treatment regimen.

Results: From January 1, 2014 to December 31, 2015, MDR screen was performed on n=603 primary clinical specimens. Of 603 primary specimens a result could not be determined for n=81 (indeterminate or positive control band for TB missing). Of the 522 primary specimens for which a result was known, 38 were RIF mono-resistant, and 39 were INH resistant. In-depth review of the MDR treatment regimen.

Objective: The Florida Department of Health Bureau of Public Health Laboratories (BPHL) utilizes the MTBDRplus assay as its molecular ‘MDR Screen’. The test can be performed directly on the specimen with a turnaround time (TAT) of approximately 8 hours. The instrumentation is inexpensive, results are easily visualized and interpreted.

This study analyzed the performance of the Hain MTBDRplus assay in our TB testing algorithm over a two-year period to determine the impact of test results on patient therapy.

Results

MDR Screen results were analyzed for 603 specimens over a 2-year period

522 clinical specimens had results that could be analyzed. Relevant mutations were detected in n=56 specimens (10.72%), Table 2.

Molecular MDR Screen

DNA sequencing: Sanger DNA sequencing was performed for confirmation of resistance mutations on a Genetic Analyzer ABI Prism 3100 (Life Technologies). Sequences were analyzed using BioNumerics software (Applied Maths) and compared to wild type sequence.

Growth-based Antimicrobial Susceptibility Testing (AST): The TREK Sensititre® plate method (Thermo Scientific) was performed with pure MTBC isolates cultured on solid media. In brief, 0.5 McFarland dilutions of isolates were diluted 100x and incubated in the presence of increasing concentrations of drug, including INH (0.06-4mcg/mL) and RIF (0.12-16 mcg/mL). The first drug level without visible growth was determined to be the minimal inhibitory concentration (MIC) and interpreted as susceptible, INH <0.25 mcg/mL, RIF ≤1 mcg/mL

Results

The average TAT for the MDR Screen was 9.44 days, the mode was 2.5 days

82.9% of all specimens tested by MDR Screen were resulted within 10 days or less from the receipt of the specimen in our laboratory and more than 55% within 5 days, the mode was 2.5 days (Table 2).

TAT for MDR Screen

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<th>11-15 days</th>
<th>&gt; 16 days</th>
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<td>(avg. 3.57)</td>
<td>(avg. 7.48)</td>
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<td>334</td>
<td>168</td>
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<tr>
<td>(55.38)</td>
<td>(27.52)</td>
<td>(3.31)</td>
<td>(13.75)</td>
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Table 2. TAT for MDR screen on clinical specimens (2014-2015)

References