Detection of \textit{katG} and \textit{inhA} mutations to guide isoniazid and ethionamide use for drug-resistant tuberculosis

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\textbf{INTRODUCTION}

Depending on the presence of mutations that determine isoniazid (INH) susceptibility (\textit{katG} and \textit{inhA}), Mycobacterium tuberculosis may be susceptible to high doses of INH or ethionamide (ETH).

\textbf{OBJECTIVE}

To describe the INH resistance profile and association of \textit{katG} mutation with previous INH treatment and level of drug resistance based on rapid molecular drug susceptibility testing (DST) in southern Brazil and central Mozambique.

\textbf{DESIGN}

Descriptive study of 311 isolates from Ribeirão Preto, São Paulo, Brazil (2011–2014) and 155 isolates from Beira, Moçambique (2014–2015). Drug resistance patterns and specific gene mutations were determined using Genotype MTBDRplus.

\textbf{Molecular Assay}

Genotype MTBDRplus version 2.0

155 HCB Moçambique 2014-2015
311 HC-FMRP-USP Brasil 2011 a 2015

\textbf{RESULTS}

\textit{katG} gene mutations were detected in 12/22 (54.5\%) Brazilian and 32/38 (84.2\%) Mozambican isolates. \textit{inhA} mutations were observed in 9/22 (40.9\%) isolates in Brazil and in 4/38 (10.5\%) in Mozambique. Both \textit{katG} and \textit{inhA} mutations were detected in respectively 1/22 (5\%) and 2/38 (5.2\%). The difference in the frequency of \textit{katG} mutations in Brazil and Mozambique was statistically significant (p=0.04). \textit{katG} mutations were present in 68.8\% (33/48) of patients previously treated with INH and 31.2\% (15/48) of patients without previous INH.

Table 1- Isoniazid patterns of resistance and frequency of \textit{inhA} and \textit{katG} mutations in \textit{M. tuberculosis} isolates from Brazil and Moçambique.

\begin{table}
\centering
\begin{tabular}{|c|c|c|c|c|}
\hline
 & \textbf{MOX-TB} & & & \\
 & \textbf{INH-R} & Total INH-resistance & & \\
 & \textbf{Brazil} & \textbf{Mozambique} & \textbf{p} & \textbf{Brazil} & \textbf{Mozambique} & \textbf{p} & \textbf{Brazil} & \textbf{Mozambique} & \textbf{p} \\
\hline
\textit{inhA} & 7 (46.6) & 2 (8.0) & 9 (40.9) & 4 (10.5) & \\
\textit{KatG} & 7 (46.6) & 22 (80.0) & 0.03 & 5 (71.4) & 0.07 & 12 (54.5) & 0.74 & 32 (84.2) & 0.04 \\
\textit{KatG/InhA} & 1 (5.8) & 1 (4.0) & 0 & 1 (7.7) & 1 (4.5) & 2 (3.3) & \\
\textit{Total} & 15 (100) & 25 (100) & 7 (100) & 13 (100) & 22 (100) & 38 (100) & \\
\hline
\end{tabular}
\caption{Previous use of INH or total latent tuberculosis infection or active TB and rate of detection of \textit{katG} and \textit{inhA} mutations.}
\end{table}

\textbf{CONCLUSION:}

INH mutations varied geographically; molecular DST can be used to guide and accelerate decision making in the use of ETH or high doses of INH to treat Drug resistant TB.

\textbf{KEY WORDS:} multidrug-resistant tuberculosis; INH resistance; molecular diagnosis; line-probe assay; mutations

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