

Ethambutol and Streptomycin Testing of Mycobacterium tuberculosis Using the Microscopic-Observation Drug-Susceptibility (MODS) Assay

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Background: The MODS assay is a rapid method for M. tuberculosis diagnosis and drug-susceptibility testing. The validity of MODS for ethambutol and streptomycin drug-susceptibility testing has been poor relative to other first-line drugs. This study aimed to improve its validity by defining the optimal critical concentration needed for these drugs.

Methods: Decontaminated sputum samples (n=48) were tested using the MODS method with concurrent serial 1:2 dilutions of ethambutol and streptomycin solutions in standard 7H9 broth. Ethambutol concentrations ranged from 20 to 0.3625 µg/mL and streptomycin from 8.0 to 0.125 µg/mL. Cultures were incubated at 37°C. M. tuberculosis growth was observed by light microscopy. Reference standard drug-susceptibility testing was done using the Tetrazolium Microplate Assay.

Results: Optimal critical concentrations for defining drug resistance in MODS were 5.0 µg/mL for ethambutol (Youden's Index: 0.68, Test efficiency: 86%) and 1.0 µg/mL for streptomycin (Youden's Index: 0.37, Test efficiency: 74%). Area under the ROC curve was 0.68 (95% CI: 0.21 to 0.96) for streptomycin and 0.87 (95% CI: 0.23 to 1.0) for ethambutol. MODS MIC₅₀ was 1.68 µg/mL for ethambutol and 2.16 µg/mL for streptomycin. MODS MIC₉₀ was 8.25 µg/mL for ethambutol and 8.85 µg/mL for streptomycin.

Conclusions: The accuracy of ethambutol and streptomycin drug-susceptibility testing in the MODS assay was improved by modifying drug critical concentrations.

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