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EDITORIAL

Rapid diagnosis of rifampicin resistance: who needs confirmation?

RAPID DRUG SUSCEPTIBILITY TESTING (DST) of rifampicin (RMP) enables timely use of a regimen that is effective in the treatment of RMP-resistant tuberculosis (TB). Two technologies currently recommended by the World Health Organization (WHO), the line-probe assay and Xpert® MTB/RIF, have the capacity for rapid DST of RMP.

In this issue of the *Journal*, Lyu and colleagues report on the performance of the Geno-Type® MTBDR*plus* assay for the detection of RMP and isoniazid (INH) resistant TB in routine practice in Korea.[1] MTBDR*plus* was 98–99% specific for both drugs; sensitivity for INH was within the expected range, and for RMP it was even slightly higher than in most previous reports (96.6%). DNA sequencing of three isolates with discordant results on slow growth-based DST revealed known RMP resistance-conferring mutations in favour of MTBDR*plus* in two (66.7%), and an *rpo*B 533Pro mutation in the third that was missed by MTBDR*plus*. Occasional failure of MTBDR*plus* to detect this mutation has been reported previously.[2]

The Korean study challenges the use of conventional DST as the reference standard for DST of RMP. Rapid growth-based DST, such as BACTEC™ MGIT™ 960, fails to detect RMP resistance due to even more frequent specific mutations.[3] The most frequent and important limitation of all rapid DST for RMP resistance is likely to be sensitivity and not specificity; confirming RMP resistance by another method may thus result in unnecessary confusion and delays.

The WHO recommends that 'patients at risk of drug resistance in whom RMP resistance is detected by Xpert should be placed on an appropriate MDR-TB [multidrug-resistant TB] regimen immediately and INH added until the DST result for INH is available'.[4] The need for confirmation of RMP resistance depends on pre-test probability, but it must also be rapid, otherwise the value of rapid DST diminishes considerably. Unfortunately, the new version of MTBDR*plus* frequently misses strains with the *rpo*B 533Pro mutation and other mutations not revealed by a specific mutation band, contrary to Xpert (AVD, unpublished data). The use of MTBDR*plus* to confirm RMP-resistant results on Xpert may thus no longer be a valid option.

Lyu and colleagues report that the median interval between test request and report was still 5.3 days for MTBDR*plus*, due to weekly batching. In the right place, Xpert would outperform MTBDR*plus* in turnaround time because batching is not needed and the results are typically available within hours. Under programme conditions, the importance of truly rapid DST to avoid losing patients prior to treatment initiation cannot be over-emphasised.

The diagnosis and treatment of MDR-TB in resource-limited settings should be as easy and straightforward as possible. Conventional DST to determine INH resistance among patients with RMP resistance followed by regimen adjustment adds complexity, and there may be no concomitant gain in increased treatment success. Routine inclusion of INH in the Bangladesh MDR-TB regimen[5] has been shown to achieve a high success rate. Wide application of simple and convenient rapid DST technology and bold use of the practical and effective Bangladesh MDR-TB treatment regimen have great potential in addressing the many challenges in the fight against MDR-TB.

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