MaHTAS
Malaysian Health Technology Assessment Section

QuantiFERON®-TB Gold
Executive Summary

[Adapted from the report by SYFUL AZLIE MD FUZI]

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Introduction

The diagnosis of latent tuberculosis infection (LTBI) is often challenged by the lack of a gold standard diagnostic test and the absence of clinical symptoms. Until recently, tuberculin skin test (TST) was the only diagnostic test available and has been widely used for diagnosis of both LTBI and active TB. However, certain limitations are associated with the use of TST. In the presence of chronic immunosuppression including autoimmune diseases, the test results may be falsely negative. In patients vaccinated against TB with Bacillus Calmette-Gue´rin (BCG) and subclinical infection with non-tuberculosis mycobacteria (NTM), the skin test may lead to false positive results. To overcome the drawbacks of TST, new in vitro assays based on interferon-γ (IFN-γ) release in response to specific *M. tuberculosis* antigens encoded in Region of Difference-1 (RD-1) have been developed. Two IFN-γ release assays (IGRAs) are currently available: the T-SPOT.TB (Oxford Immunotec, Abingdon, UK), which is based on the enzyme-linked immunospot (ELISpot) assay; and the two versions of the whole blood-based QuantiFERON®-TB (QFT) (the QFT Gold [QFT-G] and QFT Gold In-Tube [QFT-GIT] tests (Cellestis, Carnegie, Australia), which use enzyme-linked immunosorbent assay (ELISA) to detect IFN-γ in the culture supernatant. These new assay employ certain antigens like the ESAT-6 and CEP-10 (for T-SPOT.TB and QFT-G), as well as TB7.7 (only for QFT-GIT) to stimulate the production of IFN-γ from the T-cell lymphocytes. These antigens are theoretically more specific as they do not cross-react with the BCG and most NTM.

Objective/Aim

The objective of this technology review was to review evidence on the efficacy, safety and cost-effectiveness of QuantiFERON®-TB Gold as diagnostic tools for detection of patient with LTBI and active TB.

Results and Conclusions

There was fair to good level of retrievable evidence to suggest that the whole blood-based QuantiFERON®-TB (QFT) may be effective as diagnostic tools for detection of patient with LTBI and active TB. Despite the limitations, findings in general revealed that QFT appeared to have numerous advantages over TST such as higher specificity, PPV and NPV in adult population in low TB prevalence countries, better relationship with *M. tuberculosis* exposure, and lower cross-reaction rates with BCG vaccination and NTM. By using a lower cut-off value for QFT, the assay sensitivity was improved with no decrease in specificity. Malaysian Ministry of Health Clinical Practice Guidelines on Management of Tuberculosis (3rd Edition) 2012 suggested that the situations where IGRAs may be used are as the following:

i. As an alternative to TST for
   - Patients who are not expected to/could not come back for a reading of skin induration after 48-72 hours
   - Patients who had recent BCG vaccination or past NTM infection

ii. Where a 2-step test is considered (TST followed by IGRA)
   - Close-contacts whose TST is in the range of 5-9 mm
   - Patients who are offered LTBI treatment but are not convinced that they have LTBI
   - Individuals who require annual screening of LTBI (such as health care providers working in high risk areas)

There was no retrievable evidence related to adverse event of this assays. The only direct adverse effects on patient health from collecting the specimen for testing were those associated with venipuncture, namely a slight risk of bleeding, haematoma, and infection. Pain and redness at the site of injection were reported and some people became dizzy and/or faint when blood is drawn. QuantiFERON®-TB Gold on the other hand is CE marked and approved by the US FDA as an in vitro diagnostic aid for detection of *M. tuberculosis* infection. The US FDA approval notes that QFT-G is intended for use in conjunction with risk assessment, radiography and other medical and diagnostic evaluations. There was also evidence to suggest that QFT-alone was likely to be more costly but more effective than TST in Japan and United States. Analyzing cost-effectiveness is more complex because the results vary with many factors including the population being tested.

Overall, due to its higher specificity and lower cross-reaction rates with BCG vaccination and NTM, whole blood-based QuantiFERON®-TB (QFT) can be used as an alternative to TST for detection of patient with LTBI.

Methods

Literatures were searched through electronic databases specifically PubMed, Medline, Cochrane, Ovid, Horizon scanning databases, other websites; US FDA, MHRA and from non scientific database - Google search engine. In addition, a cross-referencing of the articles retrieved was also carried out accordingly to the topic. Relevant articles were critically appraised and evidence graded using US/Canadian Preventive Services Task Force.