



Role of QuantiFERON-TB Gold in diagnosis of Tuberculosis

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Abstract

Introduction: The definitive diagnosis of Tuberculosis is established when typical histological features can be demonstrated or mycobacteria can be isolated from the body fluids or from sputum or from gastric lavage. Various other methods, such as gel electrophoresis, radiometric assay and polymerase chain reaction are also available. It is well documented that isolation of mycobacteria and culture is difficult and time consuming and other tests are complex and technically more demanding. In this study, we correlated the results of QuantiFERON-TB Gold test with tuberculin skin test and sputum positivity.

Material and methods: Total 150 subjects were included in this study. The clinical features and detailed history of each case was recorded in a standard format including exposure to infection and physical examination. Patients were tested for QuantiFERON-TB Gold.

Results: The results obtained in this study showed that single method for diagnosis of tuberculosis patients may not be able to detect all the positive cases of tuberculosis. Whereas combining two methods for the diagnosis of tuberculosis patients is more advantageous way for the detection of tuberculosis patients. The combination of tuberculin skin test along with the QuantiFERON-TB Gold test had yield 96.6% cases as positive in our study which is far better than using a single test.

Conclusion: Use of QuantiFERON-TB Gold test for the diagnosis of tuberculosis is superior to conventional methods of diagnosis, above which the QuantiFERON-TB Gold test in combination with tuberculin skin test yields the maximum number of true positive cases of tuberculosis. The levels of new markers, serum interferon gamma (IFN- γ) after stimulation by foreign antigen by QFT test and combining it with tuberculin skin test yields a good amount of true positive cases of tuberculosis even in latent cases.

Key words

Interferon gamma, Sputum, Tuberculin skin test, Mycobacterium, Microscopic.

Introduction

Tuberculosis (TB) is one of the dreadful diseases affecting a number of people in developing countries including India. It is one of the most common diseases causing a high mortality and morbidity. The total number of cases is rising every year because of rapidly growing population, socio-cultural reasons, increasing number of HIV cases, increasing number of poor people and non-compliance to the treatment. Another emerging issue is widespread dissemination of multiple drug resistant cases of TB, which has raised the eyebrows of public health experts because it not only makes the disease condition more lethal, it also required very high costs to cure the condition. The definitive diagnosis is established when typical histological features can be demonstrated or mycobacteria can be isolated from the body fluids or from sputum or from gastric lavage. Various other methods, such as gel electrophoresis, radiometric assay and polymerase chain reaction are also available. It is well documented that isolation of mycobacteria and culture is difficult and time consuming and other tests are complex and technically more demanding, most of the times diagnosis is based on radiological features, clinical features and positive tuberculin testing [1]. Recently, attempts are on to find most simple techniques which are reliable, more feasible; less costly and giving quick results and are largely comparable with standard techniques. In this study, we correlated the results of QuantiFERON-TB Gold test with tuberculin skin test and sputum positivity.

Material and methods

The present study was carried out in Department of Pathology of G.S.V.M. Medical College, Kanpur from January 2008 to October 2010. Total 150 subjects were included in this

study. The clinical features and detailed history of each case was recorded in a standard format including exposure to infection and physical examination. Patients were tested for QuantiFERON-TB Gold and other routine work up including tuberculin skin test and sputum examination. The method used in our study was QFTG-IT. The statistical analysis was done accordingly with simple mathematical calculation.

Results

The results obtained from the study were tabulated and interpreted as per **Table – 1**. The combination of tuberculin skin test along with the QuantiFERON-TB Gold test had yield 96.6% cases as positive which was far better than using a single test like sputum examination (63.3%), tuberculin skin test (68%) and QuantiFERON-TB Gold (70%). It had also advantage over combining test like sputum positivity + tuberculin skin test (84.6%) while QuantiFERON-TB Gold + sputum examination (76.6%) as per **Table - 1**.

Discussion

The results obtained in this study showed that single method for diagnosis of tuberculosis patients may not be able to detect all the positive cases of tuberculosis. Whereas combining two methods for the diagnosis of tuberculosis patients is more advantageous way for the detection of tuberculosis patients. The combination of tuberculin skin test along with the QuantiFERON-TB Gold test had yield 96.6% cases as positive in our study which is far better than using a single test sputum examination (63.3%), tuberculin skin test (68%) and QuantiFERON-TB Gold (70%). It has also advantage over combining test like sputum positivity + tuberculin skin test (84.6%) while QuantiFERON-TB Gold + sputum examination (76.6%).

IFN- γ release assays (IGRAs) are exciting new developments in TB infection testing. IGRAs are based on the ability of the mycobacterium tuberculosis antigens for early secretory antigen target 6 (ESAT-6) and culture filtrate protein 10 (CFP-10) to stimulate host production of IFN- γ [2]. Because these antigens are not present in non-tuberculous mycobacteria or in any BCG vaccine variant, these tests can distinguish latent TB infection (LTBI). The blood tests QFT Gold in Tube and TSPOT. TB use these antigens to detect people with TB. Lymphocytes from the patient's blood are incubated with the antigens. These tests are called IFN- γ tests and are not equivalent. If the patient has been exposed to TB before, T lymphocytes produce IFN- γ in response. The QFT Gold in Tube uses an ELISA format to detect the whole blood production of IFN- γ with great sensitivity (89%). The distinction between the tests is that QFT Gold quantifies the total amount of IFN- γ when whole blood is exposed to the antigens (ESAT-6, CFP-10 and TB 7.7(p4)).

Due to this working principle of the QuantiFERON-TB Gold test, it is possible to detect even the latent infection in the so called healthy subjects. Miguel, et al. (2007) studied clinical utility of IFN- γ Assay in the diagnosis of TB [3]. This study discussed the potential benefits and drawbacks in patients, including those who are immune compromised. This tests that measure the production of IFN- γ by T-cells after sensitization with mycobacterium TB antigens are available and, at least theoretically, may overcome some of the limitations of the tuberculin skin test. Connell, et al. (2006) studied performance of a whole blood IFN- γ assay for detecting latent infection with mycobacterium TB in children. The study was undertaken to compare the performance of the whole blood IFN- γ assay with the tuberculin skin test in diagnosing LTTB infection or TB disease in children in routine clinical practice 106 children

with a high risk of LTBI or TB disease were enrolled in the study [4]. Nahid P, et al. (2006) proposed review on alternatives to the tuberculin skin test: IFN- γ assays in the diagnosis of mycobacterium TB infection. There were no alternatives to the tuberculin skin test for diagnosing latent TB infection. Because of advances in immunology and genomics, for the first time, an alternative has emerged in the form of T cell based IFN- γ assays, a new generation of in vitro tests of cellular immunity. These assays measure cell mediated immune response by quantifying IFN- γ released by T cells in response to stimulation by mycobacterium TB antigens. A review of current evidence on the performance of IFN- γ assays and Tuberculin Skin Test suggests that both the Tuberculin Skin Test and IFN- γ assays have advantages and limitations, and both tests appear to be useful at this time [5]. Inoue, et al. (2009) in their study found that all eight active TB patients had positive QFT results, and none of the 95 patients with negative results had active any TB. The sensitivity of the QFT reported is 100% (8 of 8) and the specificity is 89.7% (87 of 97 cases) [6]. Archip, et al. (2008) compared the QFT test with microscopic examination smear. They found that the test is more useful than microscopic studies of the smear. More ever it is also a faster and easier method for the diagnosis of TB [7]. All the above evidences shows that use of QuantiFERON-TB Gold test for the diagnosis of tuberculosis is superior to conventional methods of diagnosis, above which the QuantiFERON-TB gold test in combination with tuberculin skin test yields the maximum number of true positive cases of tuberculosis.

Conclusion

The levels of new markers, serum IFN- γ after stimulation by foreign antigen by QFT test and combining it with tuberculin skin test yields a



good amount of true positive cases of tuberculosis even in latent cases.

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Table – 1: Results of various tests for diagnosing TB.

Various tests for diagnosing TB	Positive	Negative
Sputum examination	95 (63.3%)	55
Tuberculin skin test	102 (68%)	48
QuantiFERON-TB Gold	105 (70%)	45
Tuberculin skin test + QuantiFERON-TB Gold	145 (96.6%)	05
Sputum examination + Tuberculin skin test	127 (84.6%)	23
QuantiFERON-TB Gold + Sputum examination	115 (76.6%)	35