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ORIGINAL ARTICLE

The Usefulness of the Tuberculosis Skin Test and the Interferon-gamma Release Assay in the Diagnosis of Latent Tuberculosis Infection in South Korea

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Abstract

Objectives: South Koreans receive the bacillus Calmette-Guerin (BCG) vaccination, which influence the result of the tuberculin skin test (TST); however, only a few studies have described the usefulness of the TST and interferon-γ release assay (IGRA) for diagnosing latent TB infection (LTBI). Therefore, our aim was to determine the usefulness of the TST and IGRA for diagnosing LTBI in a household contacts investigation.

Methods: We reviewed the 329 household contacts who visited Chung-Ang University Hospital (Seoul, Korea) from May 1, 2011 to February 28, 2014. To evaluate the effectiveness of TST and IGRA for the diagnosis of LTBI, we examined the concordance rate between the two tests, based on age. We also evaluated the risk factors for LTBI.

Results: The concordance rate between the two tests in individuals 0−24 years, 25−54 years, and over 55 years were 82.6% ($\kappa = 0.64$, $p < 0.01$), 68.9% ($\kappa = 0.40$, $p < 0.01$), and 68.4% ($\kappa = 0.35$, $p < 0.01$), respectively. The ratio of positive TST to negative IGRA was higher in individuals 25−44 years old, whereas the ratio of negative TST to positive IGRA was higher in individuals older than 55 years old. Based on the TST, the risk factor for LTBI was a cavity ($p < 0.01$). When using IGRA, the risk factors were contact time ($p = 0.04$) and age over 55 years old ($p = 0.02$).

Conclusion: The concordance rate between TST and IGRA was not good after the age of 25 years. The IGRA test reflects the known risk factors more exactly.

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1. Introduction

Tuberculosis (TB) remains a major public health problem in the world, especially in low- and middle-income countries. According to the World Health Organization, in 2011, there were 8.7 million new incident TB cases and 0.99 million TB deaths (just under 0.43 million human immunodeficiency virus-associated TB deaths) [1]. Tuberculosis is also a major public problem in South Korea because the incidence and mortality remain high [2]. Therefore, it is important to reduce the TB incidence by continuous tuberculosis supervising work.

The first priority in a TB prevention and control program is the identification and treatment of all people with active TB; the second priority is contact investigation to find people who are exposed to TB patients [3, 4] In South Korea since 1995, the diagnosis and treatment of latent TB infection (LTBI) in high-risk patients has been added in TB supervising work. After 2011, tuberculosis management guidelines have recommended diagnosing and treating contact patients and active TB patients. The tuberculin skin test (TST) and interferon-γ release assay (IGRA) are tests used in diagnosing LTBI. Because the TST is affected by the bacillus Calmette-Guerin (BCG) vaccination, the TST has low specificity in the BCG vaccination population. The IGRA, which measures *in vitro* interferon-γ production by T cells sensitized with the *Mycobacterium tuberculosis* antigens ESAT-6 and CFP-10, was created in 1995 and was put into practical use in 2000 [5,6] The IGRA offers better specificity (98−100%) and good sensitivity (79−97%); this test is unaffected by the BCG vaccination [7]. Therefore, IGRA is recommended for the BCG vaccination population [8−10]. South Koreans receive BCG vaccination in infancy. Therefore, the effectiveness of TST, despite its simplicity, is being questioned in South Korea. However, few studies have compared the usefulness of TST and IGRA for TB diagnosis in South Korea. In this study, we aimed to compare the positive rate of TST and IGRA in a contact investigation and to determine the risk factors for LTBI.

2. Materials and methods

2.1. Study design and participants

We performed a retrospective study at the Chung-Ang University Hospital (Seoul, Korea) between May 1, 2011 and February 28, 2014. The study participants included all patients with active TB and a household contact population during these periods. We collected demographic information, clinical data, acid-fast bacillus (AFB) sputum smears, TB cultures, the presence of cavitation on chest X-ray, TB-polymerase chain reaction, and contact time. To compare the effectiveness of TST and IGRA, we examined the positive rate and concordance rate, based on age. We also analyzed the risk factors of TST and IGRA.

2.2. Diagnosis of LTBI and active TB

Chest X-ray, IGRA, and TST were conducted on contact patients. The TST was performed on the forearm using a 2-tuberculin unit (TU) dose of purified protein derivative RT23 (0.1 mL). Indurations were measured after 48−72 hours. We defined a positive test result for an induration diameter of ≥10 mm. The interferon-γ release assay was performed using the QFT-TB Gold-In-Tube test (QFT-GIT; Cellestis Ltd, Carnegie, VIC, Australia) in accordance with the manufacturer's instructions. The results of IGRA were interpreted as positive in ≥0.35 IU/mL [11] Active TB was diagnosed, based on the presence of *M. tuberculosis* in culture, AFB in the microscopic examination of the clinical specimen, or chest X-ray suggestive of TB with response to anti-tuberculosis medications [12].

2.3. Statistical analysis

Statistical analysis was performed using SPSS version 18 (SPSS Inc., Chicago, IL, USA). The data were presented as the mean value with standard deviation. The positive rate and risk factors between TST and IGRA based on age was compared using the Chi-square test. The concordance rate between the two tests was evaluated using the κ coefficient. A value of $p < 0.05$ was considered statistically significant.

3. Results

From May 1, 2011 to February 28, 2014, 157 index cases had 329 household contacts, and the contacts performed contact investigation. Four (1.21%) contacts were diagnosed as having active TB. One contact had a positive culture and the remaining three contacts had negative cultures. The median age of the close contacts was 37.7 ± 22.2 years. More than one-half (59.6%) of the patients were female and 12 (3.8%) patients were diabetic. The positive rate of TST and IGRA were 46.4% and 45.9%, respectively. Among the 157 index patients, 43 (27.4%) patients had positive smears, 118 (75.2%) patients had positive cultures, and 22 (14.0%) patients had a cavity on their chest X-ray (Table 1).

3.1. Positive rate of TST and IGRA, according to age

The positive rate of TST of patients 25−34 years and 35−44 years was 46.3% and 63.8%, respectively. The positive rate of IGRA in patients 25−34 years and 35−44 years was 21.4% and 47.8%, respectively. In the *p* for trend value, the positive rate of TST did not tend to increase with increasing age. However, IGRA results tended to increase significantly with increasing age ($p < 0.01$; Figure 1).