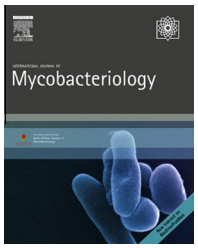
HOSTED BY

Available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/IJMYCO



Interferon-gamma release assays and tuberculin skin testing for diagnosing latent *Mycobacterium tuberculosis* infection in at-risk groups in Poland

Katarzyna Kruczak *, *Lucyna Mastalerz*, *Krzysztof Sładek*

Department of Pulmonology, Jagiellonian University Medical College, Skawinska 8, 31-066 Kraków, Poland

ARTICLE INFO

Article history:
Received 24 September 2015
Received in revised form
22 October 2015
Accepted 25 October 2015
Available online 16 November 2015

Keywords:
Latent tuberculosis infection
QuantiFERON-GIT
Tuberculin skin test
Tuberculosis

ABSTRACT

Objective/Background: The diagnostics of latent tuberculosis infection in Poland using the tuberculin skin test is challenging due to the obligatory Bacillus Calmette–Guérin vaccinations. Interferon-gamma release assays are still very rarely used for diagnostics. We compared the tuberculin skin test and the QuantiFERON-TB Gold In-Tube test to evaluate the degree of latent tuberculosis infection in at-risk groups for tuberculosis (homeless, close contacts, periodic contacts, nursing-home attendees) and in healthy individuals.

Methods: QuantiFERON-TB Gold In-Tube tests were carried out on 785 individuals from the homeless (n = 150), close contacts (n = 171), periodic contacts (n = 163), nursing-home attendees (n = 152), and healthy individuals (n = 149). The tuberculin skin test was performed on 129, 156, 147, 148, and 121 participants, respectively. We evaluated the (a) correlation between serum concentrations of interferon gamma and the tuberculin-skin-test induration diameter; (b) between the number of QuantiFERON-TB Gold In-Tube-positive results and the tuberculin-skin-test diameter in the studied groups; and (c) agreement between both tests and the kappa coefficient using the tuberculin-skin-test diameters of 5, 10, and 15 mm.

Results: Larger tuberculin-skin-test induration diameters were associated with elevated serum concentrations of interferon gamma. We found a positive correlation between the number of positive QuantiFERON-TB Gold In-Tube screening results and the tuberculin-skin-test induration diameter. The agreement between QuantiFERON-TB Gold In-Tube and tuberculin-skin-test screening results improved with increasing tuberculin-skin-test induration diameter.

Conclusion: Based on measures of tuberculin-skin-test induration diameter alone, it is difficult to diagnose latent tuberculosis infection with certainty. The agreement of the QuantiFERON-TB Gold In-Tube test increases with the tuberculin-skin-test diameter. Tuberculin-skin-test diameters larger than 15 mm are more likely to be associated with active infection.

© 2015 Asian African Society for Mycobacteriology. Production and hosting by Elsevier Ltd. All rights reserved.

* Corresponding author.
E-mail address: krucza@gmail.com (K. Kruczak).

Peer review under responsibility of Asian African Society for Mycobacteriology.
http://dx.doi.org/10.1016/j.ijmyco.2015.10.004

2212-5531/© 2015 Asian African Society for Mycobacteriology. Production and hosting by Elsevier Ltd. All rights reserved.

Introduction

It is estimated that at least 32% of the world's population (approximately 1.8 billion) is infected with *Mycobacterium tuberculosis*; the majority have asymptomatic, latent tuberculosis infection (LTBI). In countries with low and medium incidence of tuberculosis, the treatment of LTBI serves to halt the progression of this infection into the active form of the disease. This is particularly important for at-risk individuals, such as those recently infected, in close contact with a contagious patient, infected with human immunodeficiency virus (HIV), and people with previously untreated pulmonary fibrosis [1].

The tuberculin skin test (TST) is the standard method used to determine whether an individual is infected with *M. tuberculosis*. However, instances of tuberculin allergy can occur after a natural infection with the mycobacteria, or as a result of the Bacillus Calmette–Guérin (BCG) vaccine administration. For this reason, in countries (including Poland) where vaccinations, especially repeated ones, so-called revaccinations, were mandatory, the precise evaluation of the rate of mycobacterium infection using the tuberculin test is practically impossible. The immunological basis of the tuberculin test is the presence of a subset of T lymphocytes, known as *central memory cells*, which, in the event of repeated antigen presentation using tuberculin (a mixture of approximately 200 mycobacterial antigens), quickly gather and replicate to control the pathogen. The tuberculin test is not particularly specific, as the purified protein derivative is a mixture of proteins, whose antigen determinants are present in most species of mycobacteria, including the BCG vaccine. With BCG vaccinated patients and those infected with atypical mycobacteria, the so-called environmental mycobacteria, the TST result may yield a false positive [1–3]. In Poland, the National Program for Combating Tuberculosis recommends an induration diameter of at least 10 mm as positive tuberculosis skin test for the entire population (with the exception of HIV-positive patients, for whom a reaction of at least 5 mm is considered to be positive) [1–4].

Within the last few years, new methods have been developed to detect latent *M. tuberculosis* infection, such as QuantiFERON-TB Gold (Cellestis Ltd., Carnegie, Australia, now part of Qiagen) and T-SPOT.TB (Oxford Immunotec, Abingdon, Great Britain), which are highly specific and sensitive for detecting *M. tuberculosis* infection. These tests are typically peptide-based interferon-gamma (IFN-γ) assays, which measure the amount of serum IFN-γ released by specific T lymphocytes in response to antigen presentation by *M. tuberculosis* and a small number of other species of mycobacteria (*Mycobacterium kansasii*, *Mycobacterium szulgai*, and *Mycobacterium microti*). The diagnostic antigenic peptides used to induce IFN-γ release are early secretory antigenic target-6 (ESAT-6) and culture filtrate protein-10 (CFP-10), and the most recent version of the QuantiFERON-TB Gold In-Tube (QFT-GIT) test also includes the *M. tuberculosis*-specific antigen, TB7.7 [3–13]. These antigens are not present in the BCG strain bacteria, which increase the diagnostic value of these tests.

Most investigators have concluded that interferon-gamma release assays (IGRAs) have high specificity (around 62–100%, greater than TST), since these assays are not influenced by a history of BCG vaccination and infection by environmental mycobacteria. The tests are also highly sensitive; for example, the sensitivity of the enzyme-linked immunospot varies between 83% and 97%, and was higher than the enzyme-linked-immunosorbent-assay method (70–89%) [3–13]. Most studies have reported concordance at 60–90% for TST and IGRA screening tests [3,10–13]. Discordant results, TST positive/IGRA negative, are most likely associated with prior BCG vaccinations, as well as immunization with nontuberculosis environmental mycobacteria. However, it is also possible that IGRA has reduced sensitivity in specific clinical situations, as well as the limited ability to detect the immune response during certain stages of infection, for example, a recent infection that is quickly subject to spontaneous remission or responded quickly to treatment [3]. It is possible that discordant results (TST positive/IGRA negative) are associated with short incubation time of the specific mycobacterial antigens. In support of this, several studies have demonstrated that, when the incubation time using the QuantiFERON test was extended for several days, the initially negative test result returned a positive result [14]. The second type of discordant result, TST negative/IGRA positive, is more difficult to understand. It may be necessary to change the cutoff points applied so far, in order to increase the sensitivity of IGRA tests. It is also probable that the IGRA tests, as stated previously, detect recent mycobacterial infections, due to the effector T cells. (The TST screen remains negative, as central memory cells, which take part in this reaction, are not yet stimulated and do not respond with an IFN-γ release [14].) Additionally, it must be taken into consideration that, in countries with a high tuberculosis incidence, there are many factors that modulate the immunological balance of Th1/Th2, for example, malnutrition, environmental mycobacteriosis, leprosy, verminous diseases, and tropical infections [7].

In this study, we compared the QFT-GIT and TST screening methods used to detect *M. tuberculosis* in at-risk groups. The at-risk groups were the homeless, close contacts, periodic contacts, and care homeworkers, and were compared to healthy people selected at random. We analyzed the following: (a) the relationship between serum concentrations of IFN-γ and the TST induration diameters; (b) the relationship between the number of QFT-GIT-positive results and the TST induration diameter; and (c) the concordance between QFT-GIT screening results and TST induration diameter at thresholds of 5, 10, and 15 mm.

Materials and methods

Between July 2007 and September 2009, *M. tuberculosis* infection was assessed using the QFT-GIT test in four at-risk groups: 145 homeless people, 171 close contacts, 163 periodic contacts, and 152 nursing-home attendees and personnel. We tested 149 randomly selected healthy inhabitants of Kraków to serve as our control group. In total, 785 people were tested (Table 1). The tuberculin-reaction test was carried out for 129, 156, 147, 148, and 121 individuals from the aforementioned groups, respectively.

Download English Version:

https://daneshyari.com/en/article/3404987

Download Persian Version:

https://daneshyari.com/article/3404987

Daneshyari.com