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Latent tuberculosis infection among close contacts of multidrug-resistant tuberculosis patients in central Taiwan

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SUMMARY

SETTING: Both the tuberculin skin test (TST) and the QuantiFERON®-TB Gold In-Tube test (QFT-GIT) may be used to detect *Mycobacterium tuberculosis* infection. A positive reaction to either test can indicate latent tuberculosis infection (LTBI). These tests can be used to study the rate of infection in contacts of multidrug-resistant tuberculosis (MDR-TB) patients.

OBJECTIVE: To evaluate the transmission status of MDR-TB patients in Taiwan by examining their close contacts and to compare the efficiency of TST and QFT-GIT.

DESIGN: Chest radiographs, TST and QFT-GIT were performed in household contacts of confirmed MDR-TB patients to determine their infection status.

RESULTS: A total of 78 close contacts of confirmed MDR-TB patients were included in the study. The majority of the MDR-TB patients were parents of the close contacts and lived in the same building; 46% of the subjects were TST-positive and 19% were positive to QFT-GIT, indicating LTBI which was likely to develop into active MDR-TB. There was a lack of consistency between TST and QFT-GIT results in subjects with previous bacille Calmette-Guérin vaccination.

CONCLUSION: Household contacts of MDR-TB patients are likely to develop LTBI; thus, follow-up and monitoring are mandatory to provide treatment and reduce the occurrence of active infection.

KEY WORDS: latent tuberculosis; multidrug-resistant; QuantiFERON®-TB Gold In-Tube; tuberculin skin test

THE STOP TB PARTNERSHIP enhances international co-operation in TB control through its Global Plan to Stop TB. According to the World Health Organization, the control of multidrug-resistant tuberculosis (MDR-TB, defined as resistance to at least isoniazid [INH] and rifampicin [RMP]) is not as efficient as it had been hoped,[1] and it therefore remains a major threat.

Tuberculosis (TB) is an airborne transmitted infection. Close contacts of MDR-TB patients may develop MDR-TB. It is thus important to identify infected individuals, closely monitor their infection status and provide treatment to prevent the development of drug resistance.

Latent tuberculosis infection (LTBI) occurs when an individual is infected with *Mycobacterium tuberculosis*,[2] but does not present with active TB disease. Such patients nevertheless possess a 10% chance of developing TB in the future.[1] The possibility of developing TB is reduced when preventive measures are implemented.

Until recently, the tuberculin skin test (TST) was the only test available for the detection of *M. tuberculosis* infection.[2] TST can lead to false-positive reactions in bacille Calmette-Guérin (BCG) vaccinated populations and in those with non-tuberculous mycobacteria (NTM) infections.[2,3] The recent development of the QuantiFERON®-TB test (Cellestis, Carnegie, VIC, Australia) provides better screening in many instances. The QuantiFERON-TB test is based on the human body's ability to produce adaptive immunity after infection with *M. tuberculosis*.[4] The third generation of the QuantiFERON-TB test, the QuantiFERON®-TB Gold In-Tube test (QFT-GIT), uses early secreted antigenic target 6 (ESAT-6), culture filtrate protein 10 (CFP-10) and TB 7.7 as antigens to stimulate whole-blood production of the C-mode interferon.[5–7] As the antigen consists of the characteristic TB strain, the host is stimulated to release cytokines, particularly interferon-gamma (IFN-γ),[8–10] which can be used for the detection of latent infection and active disease.[11] TB infection is confirmed by the production of IFN-γ.[12]

According to the guidelines of the United States Centers for Disease Control and Prevention (CDC), LTBI can be defined as either TST or QFT-GIT positivity; both detect *M. tuberculosis* infection and existing TB infection.[2,3]

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The objective of the present study was to evaluate the transmission status of MDR-TB patients in Taiwan by examining contacts of confirmed MDR-TB patients using TST and QFT-GIT tests. The results of the two tests were also compared to determine their efficiency.

METHODS

Study population

All close household contacts of notified MDR-TB cases at Changhua Hospital from 1 June 2005 to 30 December 2007 were screened for LTBI. Seventy-eight close contacts were selected from a source of 19 index cases. The study was approved by the ethics committee of the Changhua Hospital and the Department of Health in Taiwan. Written informed consent was obtained from each subject. Subjects were informed about the aims and procedures of the study and informed of the test results at the end of the study.

Demographic information including sex, age, BCG scar, residence, medical history, history of TB contact was collected from the subjects. Chest X-ray, QFT-GIT and TST were performed for each subject.

Definition of close contacts and index cases

Close household contacts were living in the same house as an index case. MDR-TB patients had shared the same kitchen with the contacts for at least 3 months before treatment.

Nineteen MDR-TB index cases were identified under the DOTS-plus programme at the Department of Health of Changhua Hospital: 17 were men (90%) and two were women (10%), with a mean age of 61.9 years (range 28–82). Nine patients were sputum culture negative and 10 were positive. The duration of exposure was calculated as the period from the onset of active TB symptoms in the index case to the end of the LTBI evaluation. The average duration of exposure for the culture-negative ($n = 9$) and culture-positive patients ($n = 10$) was respectively 13 and 34 months. Of the 19 MDR-TB patients, six had completed treatment, with an average treatment duration of 26.5 months; the average treatment time for the remaining 13 patients was 43.7 months. The percentage of resistance to different drugs in the index cases were as follows: RMP 94.7% (18/19), INH 84.2% (16/19), ethambutol (EMB) 36.8% (7/19) and streptomycin (SM) 26.3% (5/19).

Sample collection and measurement

The QFT-GIT test was performed according to the manufacturer's recommendations.[4] Whole blood was collected into 1) a nil negative control tube (i.e., 1 ml whole blood without antigen or mitogen), 2) a TB antigen tube (i.e., 1 ml whole blood containing ESAT-6, CFP-10 and TB 7.7) and 3) a mitogen-positive control tube (i.e., 1 ml whole blood stimulated with mitogen) for each subject. The tubes were incubated at 37°C for 16–24 h. After centrifuging for 15 min, the harvested plasma was stabilised and refrigerated for at least 4 weeks. The conjugate was then added with plasma samples and standards to an enzyme-linked immunosorbent assay plate and incubated for 120 min at room temperature. The resultant sample was washed and substrate was added. The absorbance was read and interpreted after 30 min.

The results were calculated using QFT-GIT software. A positive result was interpreted as an IFN-γ level in the sample, after stimulation with ESAT-6 and CFP-10, of ⩾0.35 international units (IU)/ml; a negative result was defined as a value of <0.35 IU/ml or the mitogen tube minus Nil value ⩾0.5 IU/ml; the result was indeterminate when the mitogen value minus Nil value was <0.5 IU/ml or when the Nil value was >8.0 IU/ml.

The TST (purified protein derivative [PPD] skin test) was carried out 2 weeks after blood collection for QFT-GIT, and two-step testing (4 weeks between the first and second PPD tests) was performed to prevent an anamnestic response (i.e., the booster effect). PPD RT23 with 2 tuberculin units (TU)/0.1 ml Mantoux test was used. The diameter of the induration was read and recorded 48–72 h after intradermal injection. Technicians trained in the BCG vaccination programme carried out the TSTs and read and recorded the results. A 10-mm TST response was used as the cut-off. An induration of ⩾10 mm was recorded as a positive result.

Statistical analysis

Descriptive statistics and chest X-ray were used to determine the prevalence of TB infection. QFT-GIT and TST results and the results for BCG-vaccinated and non-BCG-vaccinated subjects were compared. Kappa (κ) statistics were used to measure the level of consistency of QFT-GIT and TST. The Mann-Whitney U-test was used to assess the difference between the two tests. Risk factors were analysed using the χ^2 test.

RESULTS

Of a total of 78 subjects, 38 were men (49%) and 40 were women (51%), with a mean age of 35.6 years. Most of the 78 subjects had been BCG vaccinated (69/78, 89%). The majority of the index cases were parents of the contacts (38/78, 49%). Forty contacts (51%) had lived with the index case for 10–20 years, and 51 (65%) lived in the same building as the index case. Of the 78 subjects, 27 (35%) had an abnormal chest X-ray but none presented with active TB, and sputum examinations were therefore not performed. Nine subjects had lung fibrosis, and 23 had other lung diseases. Of the 78 subjects, 3 had diabetes, 5 had chronic hepatitis, 2 had hypertension and 1 had another chronic disease.

Sixty-three (81%, 63/78) subjects were QFT-GIT

negative, while 15 (15/78, 19%) were positive; 42 (42/78, 54%) were TST-negative and 36 (36/78, 46%) were TST-positive. Of the 36 TST-positive subjects, 33 had been BCG-vaccinated and 3 had not (Table 1).

Table 1 QFT-GIT test and TST results in the study group

	BCG		
	Non-vaccinated ($n = 9$) *n* (%)	Vaccinated ($n = 69$) *n* (%)	Total *n* (%)
QFT-GIT			
Negative	7 (78)	56 (81)	63 (81)
Positive	2 (22)	13 (19)	15 (19)
TST			
Negative*	6 (67)	36 (52)	42 (54)
Positive†	3 (33)	33 (48)	36 (46)

*TST <10 mm.
†TST ⩾10 mm.
QFT-GIT = QuantiFERON®-TB Gold In-Tube; TST = tuberculin skin test; BCG = bacille Calmette-Guérin.

Thirty-nine subjects were both QFT-GIT and TST negative; 24 were TST-positive but QFT-negative; three were TST-negative but QFT-positive; and 12 were positive for both tests (Table 2). On comparing the QFT-GIT and TST results, the consistency of the two tests in nine non-vaccinated subjects was 89% ($\kappa = 0.73$, $P < 0.05$), while a 62% correlation between the two tests was found in those who were vaccinated ($\kappa = 0.23$, $P < 0.02$; Table 3). Statistical analysis, however, showed significant correlation between the two tests ($P < 0.05$).

QFT-GIT-positive subjects were found to have significantly higher TST results than QFT-GIT-negative subjects despite their vaccination status (Mann-Whitney U test, $P < 0.001$; Table 4).

None of the factors investigated, including kinship, length of time spent together and level of contact with an index case, were seen to affect QFT-GIT results and relatively high relative risk values (Table 5). The

Table 2 QFT-GIT and TST results vs. BCG vaccination status in the study group

	QFT-GIT test				
	Negative ($n = 63$)		Positive ($n = 15$)		
	TST negative* *n* (%)	TST positive† *n* (%)	TST negative* *n* (%)	TST positive† *n* (%)	*P* value
BCG					
Non-vaccinated ($n = 9$)	6 (67)	1 (11)	0	2 (22)	0.083
Vaccinated ($n = 69$)	33 (48)	23 (33)	3 (4)	10 (15)	0.043‡
Total ($n = 78$)	39 (50)	24 (31)	3 (4)	12 (15)	
M. tuberculosis infection	Not infected	May be infected	May be infected (anergic)	High probability of infection	

*TST <10 mm.
†TST ⩾10 mm.
‡$P < 0.05$.
QFT-GIT = QuantiFERON®-TB Gold In-Tube; TST = tuberculin skin test; BCG = bacille Calmette-Guérin.

Table 3 Consistency of QFT-GIT and TST

	TST/QFT-GIT test						
	–/–	–/+	+/–	+/+	Kappa	*P* value	Agreement %
BCG							
Non-vaccinated ($n = 9$)	6	0	1	2	0.73	0.023*	89
Vaccinated ($n = 69$)	33	3	23	10	0.23	0.020*	62

*$P < 0.05$.
QFT-GIT = QuantiFERON®-TB Gold In-Tube; TST = tuberculin skin test; BCG = bacille Calmette-Guérin.

Table 4 Comparison of QFT-GIT test and TST results (Mann-Whitney *U*-test)

	TST					
QFT-GIT test	*n*	Mean,* mm	SD	Minimum	Maximum	*P* value
BCG						
Non-vaccinated ($n = 9$)						
Negative	7	3.14	5.43	0	14	
Positive	2	12.50	0.71	12	13	
Vaccinated ($n = 69$)						
Negative	56	7.79	5.30	0	20	0.001*
Positive	13	14.69	6.17	0	24	

*$P < 0.05$.
QFT-GIT = QuantiFERON®-TB Gold In-Tube; TST = tuberculin skin test; SD = standard deviation; BCG = bacille Calmette-Guérin.

Table 5 Relationship between demographic data and QFT-GIT and TST results

	QFT-GIT					TST			
	n (%)	Negative* *n*	Positive† *n* (%)	RR	*P* value	Negative* *n*	Positive† *n* (%)	RR	*P* value
Sex									
Male	38 (49)	29	9 (23.7)			21	17 (44.7)		
Female	40 (51)	34	6 (15.0)	0.60	0.50	21	19 (47.5)	1.06	0.99
Age, years									
⩽30	33 (42)	27	6 (18.2)			23	10 (30.3)		
31–50	28 (36)	23	5 (17.9)	1.00	1.00	11	17 (60.7)	2.00	0.03‡
>50	17 (22)	13	4 (23.5)	1.30	0.70	8	9 (52.9)	1.75	0.21
Symptoms									
None	77 (99)	62	15 (19.5)			42	35 (45.5)		
Cough >2 weeks	1 (1)	1	0			0	1		
Kinship									
Spouse	11 (14)	8	3 (27.3)			5	6 (54.5)		
Parent	38 (49)	31	7 (18.4)	0.68	0.67	18	20 (52.6)	0.96	1.00
Grandparent	20 (26)	18	2 (10.0)	0.37	0.32	14	6 (30.0)	0.55	0.26
Sibling	1 (1)	1	0	0.00		1	0	0.00	
Child	4 (5)	2	2 (50.0)	1.83	0.56	1	3 (75.0)	1.38	0.60
Relative	3 (4)	2	1 (33.3)	1.22	1.00	3	0	0.00	
Friend	1 (1)	1	0	0.00		0	1 (100.0)	1.83	
Length of time spent together, years									
<10	15 (19)	9	6 (40.0)			9	6 (40.0)		
10–20	40 (51)	36	4 (10.0)	0.25	0.09	21	19 (47.6)	1.19	0.85
>20	23 (30)	18	5 (21.7)	0.54	0.69	12	11 (47.8)	1.20	0.89
Level of contact									
Living in the same building	51 (66)	39	12 (23.5)			28	23 (45.1)		
Using the same kitchen >3 months	1 (1)	1	0	0.00		0	1		
Spending >8 h in the same environment	13 (17)	11	2 (15.4)	0.65	0.72	6	7 (53.8)	1.19	0.80
Occasional	13 (17)	12	1 (9.1)	0.39	0.43	8	5 (36.4)	0.81	0.74

*<10 mm.
†⩾10 mm.
‡$P < 0.05$.
QFT-GIT = QuantiFERON®-TB Gold In-Tube; TST = tuberculin skin test; RR = relative risk.

majority of the demographic factors failed to show any significant effect on TST results. The 31–50 year age group was the only factor to have a statistically significant effect on TST results.

DISCUSSION

We found that previous BCG vaccination significantly affected QFT-GIT and TST results. In the nine non-BCG-vaccinated subjects, the percentage of positive results for the two tests was similar (QFT-GIT 2/9, 22% vs. TST 3/9, 33%). However, in the 69 BCG vaccinated subjects, the difference between the two tests was greater: 13/69 (19%) were QFT-GIT-positive and 33/69 (48%) were TST-positive. This indicated that the PPD antigen used in TST led to false-positive results in BCG-vaccinated subjects and in those with NTM infection. Overall, 36 subjects (46%) were TST-positive, and 15 (19%) were QFT-GIT-positive. There seemed to be an inconsistency in the results of the two tests. Nevertheless, similar findings were reported in a study carried out in Melbourne, Australia, where there were fewer positive QFT-GIT results (6.7%) than TST results (33%).[13]

As both TST and QFT measure the presence of *M. tuberculosis*, our results could be interpreted as follows:

1 Absence of mycobacterial infection: 39 subjects in our study were not infected, as both TST and QFT were negative.
2 Possible mycobacterial infection: a positive TST result with a negative QFT reaction may be due to previous exposure to NTM or history of BCG vaccination for which an organism closely related to the tubercle bacillus, *M. bovis*, is used as an antigen. Either could have led to a false-positive reaction.[14]
3 Anergy: negative TST but positive QFT may indicate that the subject has TB infection, but that the TST is false-negative. This could occur especially in the case of immunosuppression or natural waning of immunity, or due to the effect of NTM such as *M. kansasii, M. marinum* or *M. szulgai*[14] on QFT.
4 A high probability of infection: both tests indicated the presence of *M. tuberculosis*, and therefore the 12 subjects with positive results to both tests from our study needed close follow-up.

Similar results were noted in a study conducted by Mahomed et al. in 2006, who compared the TST with the three generations of QuantiFERON tests.[6] They also reported a lack of consistency between the TST and QFT results and between the different generations of QuantiFERON tests. The rates of positivity for the different tests varied from 81% for the TST (10 mm as cut-off point), 60% for QFT, 38% for QFT-G to 56% for QFT-GIT. These results suggested that the extra *M. tuberculosis*-specific antigen used in the QFT-GIT method (TB antigen 7.7), or the immediate incubation of whole blood at 37°C after collection had increased the sensitivity of the QFT-GIT test as compared to the other generations. The correlation of the tests for BCG-vaccinated individuals in the study by Mahomed et al. was 69% (κ = 0.32), comparable to our result of 62% (κ = 0.23). A Korean study also found that the sensitivity of QFT-GIT in the diagnosis of LTBI infection was higher than that of TST in immunocompromised patients.[10]

Both TST and QFT have advantages and disadvantages. The drawbacks of TST include the need for patients to return for test reading, a frequent reading bias, variability in test application, booster effect, false-negative results due to intercurrent immunosuppression, and low specificity in previously BCG-vaccinated subjects. The QFT test performs better in these aspects, but requires blood collection, processing within 12 h of collection, and it lacks sensitivity to previous infections. In addition, QFT is relatively more expensive and requires technicians with specific laboratory skills and experience;[14] as a result, increased costs are involved for screening large numbers of close contacts of confirmed MDR-TB patients.

The US CDC recommends a 6–9 month LTBI regimen with INH for high-risk subjects, such as those with human immunodeficiency virus infection or organ transplant recipients with positive QFT or TST results.[2,3] The German Central Committee Against Tuberculosis, however, recommends confirming positive TST results using an interferon-gamma release assay (QFT or T-SPOT.*TB*) before offering LTBI treatment.[15] In our study, no treatment was given to any of our subjects, as our research involved close contacts of MDR-TB patients and second-line drugs are generally more toxic. After reviewing their symptoms, risk assessment, radiography and other medical and diagnostic evaluations, it was decided that more precise verification was needed to confirm active TB infection. Treatment was therefore not indicated at this stage. However, regular chest X-rays and follow-up of these subjects were undertaken, and to date no active TB has been reported.

The Taiwanese Center for Disease Control implemented the DOTS-Plus programme in May 2007, and it was hoped that with this active treatment programme and strict supervision of MDR-TB patients, patients could be treated early and the risk for disease transmission reduced. Contacts who are already infected should be closely monitored and treated as soon as possible. In terms of prevention, it is still difficult to determine suitable treatment due to the likelihood of a drug-resistant strain presenting in contacts of MDR-TB patients.

CONCLUSION

In a total of 78 patients, 46% were TST-positive and 19% were QFT-GIT-positive. Twelve (15%) were positive with both tests. Both TST and QFT-GIT can be used to detect TB disease or LTBI. As they do not measure the same components of the immunological response, they are not interchangeable. Both tests should be used in conjunction with risk assessment, radiography and other medical and diagnostic evaluations. The QFT-GIT test can be especially useful, and more specific than TST, in detecting LTBI in countries such as Taiwan, which has high BCG vaccination coverage.

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References

1 World Health Organization. Drug and multidrug-resistant tuberculosis (MDR-TB). Geneva, Switzerland: WHO, 2009. http://www.who.int/tb/challenges/mdr/en/index.html Accessed December 2009.

2 Mazurek G H, Villarino M E. Guidelines for using the QuantiFERON®-TB test for diagnosing latent *Mycobacterium tuberculosis* infection. Centers for disease control and prevention. MMWR 2003; 52 (RR02): 15–18.

3 Mazurek G H, Jereb J, LoBue P, Iademarco M F, Metchock B, Vernon A. Guidelines for using the QuantiFERON-TB gold test for detecting *Mycobacterium tuberculosis* infection, United States. Centers for Disease Control and Prevention. MMWR 2005; 54 (RR15): 49–55.

4 Cellestis. QuantiFERON-TB Gold In-Tube method and technical information. Melbourne, VIC, Australia: Cellestis, 2009. http://www.cellestis.com/IRM/Content/aust/qtfproducts_tbgoldintube_techinfo.html Accessed December 2009.

5 Pollock J M, McNair J, Bassett H, et al. Specific delayed-type hypersensitivity responses to ESAT-6 identify tuberculosis-infected cattle. J Clin Microbiol 2003; 41: 1856–1860.

6 Mahomed H, Hughes E J, Hawkridge T, et al. Comparison of Mantoux skin test with three generations of a whole blood IFN-γ assay for tuberculosis infection. Int J Tuberc Lung Dis 2006; 10: 310–316.

7 Brock I, Munk M E, Kok-Jensen A, Andersen P. Performance of whole blood IFN-γ test for tuberculosis diagnosis based on PPD or the specific antigens ESAT-6 and CFP-10. Int J Tuberc Lung Dis 2001; 5: 462–467.

8 Vordermeier H M, Chambers M A, Cockle P J, Whelan A O, Simmons J, Hewinson R G. Correlation of ESAT-6-specific gamma interferon production with pathology in cattle following *Mycobacterium bovis* BCG vaccination against experimental bovine tuberculosis. Infect Immun 2002; 70: 3026–3032.

9 Teixeira L, Perkins M D, Johnson J L, et al. Infection and disease among household contacts of patients with multidrug-resistant tuberculosis. Int J Tuberc Lung Dis 2001; 5: 321–328.
10 Kim E Y, Lim J E, Jung J Y, et al. Performance of the tuberculin skin test and interferon-γ release assay for detection of tuberculosis infection in immunocompromised patients in a BCG-vaccinated population. BMC Infect Dis 2009; 9: 207.
11 Katial R K, Hershey J, Purohit-Seth T, et al. Cell-mediated immune response to tuberculosis antigens: comparison of skin testing and measurement of in vitro gamma interferon production in whole-blood culture. Clin Diagn Lab Immunol 2001; 8: 339–345.
12 Kobashi Y, Obase Y, Fukuda M, Yoshida K, Miyashita N, Oka M. Clinical reevaluation of the QuantiFERON TB-2G test as a diagnostic method for differentiating active tuberculosis from non-tuberculous mycobacteriosis. Clin Infect Dis 2006; 43: 1540–1546.
13 Vinton P, Mihrshahi S, Johnson P, et al. Comparison of QuantiFERON-TB Gold In-Tube test and tuberculin skin test for identification of latent *Mycobacterium tuberculosis* infection in healthcare staff and association between positive test results and known risk factors for infection. Infect Control Hosp Epidemiol 2009; 30: 215–221.
14 Kunst H. Diagnosis of latent tuberculosis infection: the potential role of new technologies. Respir Med 2006; 100: 2098–2106.
15 Diel R, Loddenkemper R, Meywald-Walter K, et al. Comparative performance of tuberculin skin test, QuantiFERON-TB Gold In-Tube Assay, and T-SPOT.*TB* test in contact investigations for tuberculosis. Chest 2009; 135: 1010–1018.

RÉSUMÉ

CONTEXTE : Pour la détection de l'infection par *Mycobacterium tuberculosis*, on peut utiliser à la fois le test cutané tuberculinique (TST) et le test QuantiFERON®-TB Gold In-Tube (QFT-GIT). Une réaction positive à l'un ou l'autre de ces tests correspond à une infection tuberculeuse latente (LTBI). Ces tests peuvent être utilisés pour investiguer le taux d'infection chez les contacts de patients atteints de tuberculose à germes multirésistants (TB-MDR).

OBJECTIF : Evaluer à Taiwan le statut de transmission des patients TB-MDR en examinant leurs contacts étroits, et comparer l'efficacité des TST et QFT-GIT.

SCHÉMA : On a réalisé des clichés thoraciques, des TST et des QFT-GIT chez les sujets en contact au domicile avec des patients atteints de TB-MDR confirmée afin de connaître leur statut en matière d'infection.

RÉSULTATS : On a inclus au total 78 contacts étroits de patients atteints de TB-MDR. La majorité des patients TB-MDR étaient des parents des contacts étroits et vivaient dans le même bâtiment. Le TST a été positif chez 56% des sujets et le test QFT-GIT chez 19%. Ceux-ci étaient atteints de LTBI et susceptibles de développer ultérieurement une TB-MDR active. Il existe un manque de cohérence entre les résultats du TST et ceux du QFIT chez les sujets vaccinés antérieurement par le bacille Calmette-Guérin.

CONCLUSION : Comme les contacts au domicile des patients TB-MDR sont susceptibles de développer la LTBI, un suivi et une surveillance sont indispensables pour leur fournir un traitement et réduire l'apparition d'une infection active.

RESUMEN

MARCO DE REFERENCIA: La prueba cutánea de la tuberculina (TST) y la prueba QuantiFERON®-TB Gold En Tubo (QFT-GIT) se pueden utilizar en la detección de la infección por *Mycobacterium tuberculosis*. Una reacción positiva a alguna de estas pruebas refleja una infección tuberculosa latente (LTBI). Estos ensayos se pueden usar con el propósito de investigar la tasa de infección en los contactos de los pacientes con tuberculosis multidrogorresistente (TB-MDR).

OBJETIVO: Se buscó evaluar la situación de la transmisión en los pacientes con MDR-TB en Taiwán, al examinar sus contactos cercanos y comparar la eficacia diagnóstica de la TST y las pruebas QFT.

MÉTODO: Con el propósito de definir el estado de contagiosidad, se practicaron la radiografía de tórax, la TST y la prueba QFT a los contactos domiciliarios de los pacientes con TB-MDR confirmada.

RESULTADOS: Participaron en el estudio 78 contactos cercanos de pacientes con TB-MDR confirmada. La mayoría de los pacientes con TB-MDR eran familiares de sus contactos cercanos y residían en el mismo edificio. El cuarenta y seis por ciento de las personas tuvo una reacción TST positiva y el 19% resultados positivos en la prueba QFT. Estas personas presentaban una LTBI y existía la posibilidad de que evolucionaran hacia una TB-MDR activa. Se observó incongruencia entre los resultados de ambas pruebas en las personas con antecedente de vacunación antituberculosa.

CONCLUSIÓN: Los contactos domiciliarios de pacientes con TB-MDR pueden contraer una LTBI, por lo cual es obligatorio practicar el seguimiento y la vigilancia de estas personas, con el propósito de suministrar el tratamiento necesario y disminuir la transmisión activa de la enfermedad.