Tuberculin skin test: operational research in the state of Mato Grosso do Sul, Brazil*

Teste tuberculínico: pesquisa operacional no Mato Grosso do Sul

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Abstract

Objective: To investigate operational aspects of tuberculin skin test (TST) use in tuberculosis control programs and at specialized Brazilian National Sexually Transmitted Diseases/AIDS and Viral Hepatitis Program health care clinics in priority municipalities for tuberculosis control in the state of Mato Grosso do Sul, Brazil. **Methods:** This was a descriptive, cross-sectional, epidemiological survey. Data on qualifications/training of professionals administering TSTs, timing of the TST, procedures in cases of loss to follow-up (reading), material availability, and material storage were collected through interviews and technical visits. For the 2008-2009 period, we determined the numbers of screenings in vulnerable populations, of TSTs performed, and of patients treated for latent tuberculosis. **Results:** We interviewed 12 program managers in six municipalities. Some programs/clinics did not perform TSTs. Nursing teams administered the TSTs, results were read by non-specialists, and specialization/refresher courses were scarce. The PPD RT23 was stored in 5-mL flasks under appropriate conditions. Insulin syringes were commonly used. Testing was available during business hours, three times a week. In cases of loss to follow-up, telephone calls or home visits were made. Of the 2,305 TSTs evaluated, 1,053 (46%) were performed in indigenous populations; 831 (36%) were screenings in prisons, performed for training; and only 421 (18%) involved contacts of tuberculosis patients or vulnerable populations. Four vulnerable patients and 126 indigenous subjects were treated for latent tuberculosis. **Conclusions:** These priority municipalities showed operational difficulties regarding human resources, materials, and data records.

Keywords: Tuberculin test; Health services research; HIV; Latent tuberculosis; Chemoprevention.

Resumo

Objetivo: Investigar a operacionalização da utilização do teste tuberculínico (TT) em programas de controle de tuberculose e em serviços de assistência especializada do Programa Nacional de Doenças Sexualmente Transmissíveis/AIDS e Hepatites Virais em municípios prioritários para o controle da tuberculose no estado de Mato Grosso do Sul. **Métodos:** Estudo epidemiológico descritivo, transversal, do tipo inquérito. A formação profissional dos responsáveis pela realização do TT, existência de treinamentos, período de realização dos TTs, conduta em caso de perda de leitura, insumos disponíveis e sua conservação foram levantados por meio de entrevistas e visitas técnicas. O número de inquéritos em populações vulneráveis, número de TTs realizados e número de pacientes em tratamento de tuberculose latente entre 2008 e 2009 foram também levantados. **Resultados:** Foram entrevistados 12 gestores de seis municípios. Alguns programas/serviços não realizavam o TT. A equipe de enfermagem realizava os TTs, não havia leitores especialistas, e treinamentos eram raros. A conservação dos frascos de PPD RT23 (5 mL) era adequada. Frequentemente utilizava-se a seringa de insulina. A realização de TT ocorria no horário comercial, três vezes na semana. Em caso de perda de leitura em alguns locais, realizava-se contato telefônico ou visita domiciliar. O total de TT realizados foi de 2.305, dos quais 1.053 (46%) foram realizados em populações indígenas, 831 (36%) foram realizados em ambientes prisionais para fins de treinamento (inquéritos), e apenas 421 (18%) foram realizados em contatos de pacientes com tuberculose e em populações vulneráveis. O tratamento de tuberculose latente foi realizado em 4 pacientes vulneráveis e em 126 indígenas. **Conclusões:** Os municípios prioritários demonstraram dificuldades operacionais em relação a recursos humanos, insumos e registros de informação.

Descritores: Teste tuberculínico; Pesquisa sobre serviços de saúde; HIV; Tuberculose latente; Quimioprevenção.

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Introduction

Latent tuberculosis affects approximately one third of the world population, and it has been estimated that the annual risk of progression to active tuberculosis among HIV-infected individuals is as high as 10%, tuberculosis therefore being the most common opportunistic disease and the leading cause of death among HIV-infected individuals worldwide.[1]

The tuberculin skin test (TST) is one of the tools for the identification of latent tuberculosis and is an ancillary test for the diagnosis of active tuberculosis. The results of the TST guide the therapeutic approach to latent tuberculosis.[2-6] The TST is performed by the Mantoux method, which consists of the administration of 0.1 mL (2 TU) of PPD RT23 on the volar aspect of the forearm. The results of the test are read within 48-72 h after PPD RT23 administration.[4,7,8] Individuals with an induration ≥ 10 mm are considered infected. However, in immunocompromised individuals, the cut-off induration value has been set at 5 mm.[7]

Strategies to reduce the incidence of tuberculosis in HIV-infected individuals include the preventive use of isoniazid in patients with latent tuberculosis, the initiation of antiretroviral therapy, and measures aimed at preventing the transmission of the disease in the community by detecting active cases as early as possible.[1,8] The preventive approach prioritizes individuals who are immunocompromised or are receiving immunosuppressive therapy, children younger than two years of age, and the elderly, as well as health care workers and medical students, who are at a higher risk of becoming infected because of occupational exposure.[9-13]

Latent tuberculosis treatment with isoniazid plays a fundamental role in tuberculosis control and can prevent active tuberculosis in 60-90% of the cases.[13,14] Operational difficulties in identifying latent tuberculosis constitute major obstacles to the implementation of preventive therapy with isoniazid.[15]

The objective of the present study was to investigate operational aspects of TST use in tuberculosis control programs (TCPs) and at primary care clinics (PCCs) affiliated with the Brazilian National Sexually Transmitted Disease (STD)/AIDS and Viral Hepatitis Program in priority municipalities for tuberculosis control in the state of Mato Grosso do Sul, Brazil.

Methods

This was a descriptive, cross-sectional, epidemiological survey. On the basis of tuberculosis control data and epidemiological markers, we chose six priority municipalities in the state of Mato Grosso do Sul. The survey was conducted between May and June of 2010.

We interviewed six municipal coordinators of TCPs; four managers of specialized TCP-affiliated PCCs in five priority municipalities, including a specialized PCC that provides treatment to patients in two priority municipalities; one state coordinator of a TCP; and one state coordinator of the Brazilian National STD/AIDS and Viral Hepatitis Program. One of the investigators made a technical visit to each of the facilities.

For each municipality, we collected data regarding the principal operational aspects of TST use, including the organization of the facility (human resources, materials, and patient access to the test) and TST administration indicators (screenings, number of TSTs performed, and number of patients treated for latent tuberculosis). When there were no records or information regarding certain operational aspects of TST use, we asked why the test had not been performed.

The interviews covered the following: qualifications/training of professionals administering TSTs and reading TST results; availability of materials; days of the week on which TSTs were performed; and procedures in cases of loss to follow-up (reading). For the 2008-2009 period, we determined the numbers of screenings in vulnerable populations, of TSTs performed, and of patients treated for latent tuberculosis.

Secondary information sources were TST registries (if available), patient registries, and registries of the follow-up treatment of tuberculosis cases, as well as TST results registered in medical charts or in the Brazilian Case Registry Database (for tuberculosis and AIDS cases).

The study was approved by the Human Research Ethics Committee of the Federal

University of Mato Grosso do Sul (Protocol no. 1722).

Results

The six municipalities under study shared one characteristic: the TCP and immunization program nursing teams were responsible for administering the TST. In general, the TST was administered by nurse technicians or by TCP managers (nearly all of whom were nurses), as can be seen in Chart 1. In all of the priority municipalities evaluated, all of the TSTs performed were provided by TCPs. Of the four managers of the specialized PCCs in the priority municipalities under study, one declined to participate in the study. Of the three specialized PCCs under study, only two offered TSTs.

In the capital of the state, the decentralization of the TCP to the health districts resulted in the TST being administered by the nursing staff of PCCs affiliated with the Family Health Program. The Campo Grande TCP manager reported that, including the screenings in prisons and the tests performed in two specialized PCCs, 169 TSTs were performed. All of the health care workers stated that they learned how to administer the TST through professional experience. Health care workers had reportedly received training in how to administer the TST during BCG vaccination training courses. Our survey revealed that there were no training courses for the health care workers at the specialized PCCs under study; however, in the 2008-2009 period, there was, via four of the TCPs, at least one training course for the health care workers who administered the TST to prison or penitentiary inmates.

It was reported that, via the Mato Grosso do Sul State TCP, two training courses were held at prisons in the state capital in 2009. The courses provided training to 26 health care workers in two priority municipalities. The principal objectives of the training courses were to improve the TST administration technique and to standardize the reading of TST results. Neither of the municipalities had health care workers that specialized in reading TST results.

Tuberculin syringes were used by all but one TCP. In that case, the procedure was performed with insulin syringes, available via the immunization program. At the specialized PCCs, the syringes that were most commonly used were insulin syringes. Tuberculin syringes were used at only one specialized PCC.

In all of the municipalities under study, PPD RT23 was stored in 5-mL flasks under appropriate, temperature-controlled conditions, i.e., in refrigerators, which were also used to store the vaccines administered via the local immunization program. In one of the municipalities, we found flasks that had remained open for more than 30 days and were past their expiration date.

Testing was available during business hours (from 7:00-11:00 a.m. and from 1:00-5:00 p.m.), three times a week. There was no repressed demand for TSTs. At the specialized

Chart 1 - Operational aspects evaluated and results obtained in the priority municipalities for tuberculosis control in the state of Mato Grosso do Sul, 2008-2009.

Operational aspects evaluated	Results
Professionals responsible for administering TSTs	Nursing staff
Training	No specialists in reading TST results
TST hours available	Business hours on weekdays (no repressed demand)
Procedures in cases of loss to follow-up	Home visits, via four of the TCPs; telephone calls, via five of the TCPs; and no strategies to counter loss to follow-up at the specialized PCCs
PPD RT23 storage container (5 mL-flask)	Appropriately stored in refrigerators that were also used to store vaccines
Records of TST results	No specific registries of TST results
Type of syringe used in order to perform the test	Tuberculin syringes at 1 specialized PCC and insulin syringes at 5 specialized PCCs
	Tuberculin syringes via 5 TCPs
Screenings in health care students/workers	None

TST: tuberculin skin test; TCP: tuberculosis control program; and PCC: primary care clinic.

PCCs, no specific protocol was followed when patients failed to return for the reading of the TST results. However, our survey revealed that, if tested via the TCPs of five of the municipalities under study, such patients were contacted by telephone, whereas those tested via the TCPs of four of the municipalities under study were visited at home.

None of the specialized PCCs had any record of the number of TSTs performed. For the tests performed via the TCPs, we counted all of the tests that had been recorded in the patient registries, as well as those that had been recorded in the registries of the follow-up treatment of tuberculosis cases. Information sources such as TST registries were nonexistent; the results were available exclusively in the medical charts of the patients.

A survey conducted at a referral center for the outpatient treatment of HIV-infected individuals in Campo Grande revealed that 113 (80.7%) of the 140 patients followed in the 2008-2009 period had never had a TST. Among those patients, the median duration of outpatient follow-up was 8 years. At the time, the facility had no professionals who were trained in administering TSTs, stored none of the materials required in order to perform TSTs, and had no isoniazid on hand. According to the facility records, as of 2009, no patients had been treated for latent tuberculosis.

Four of the TCPs had no records of patients treated for latent tuberculosis during the study period (2008-2009). According to the records, the specialized PCCs affiliated with those TCPs had treated only two cases of latent tuberculosis during that same period. Among all of the PCCs affiliated with those TCPs, a total of 4 patients were treated for latent tuberculosis during the study period.

In the priority municipalities for tuberculosis control, 421 TSTs were reported to have been performed, collectively, via the TCPs and at the specialized PCCs. Of the 2,305 TSTs performed, 1,053 (46%) were performed in indigenous populations; 831 (36%) were screenings in prisons, performed for training; and only 421 (18%) involved contacts of tuberculosis patients or priority populations, such as HIV-infected individuals.[16] In the indigenous populations, the TSTs resulted in 124 patients being treated for latent tuberculosis, a figure that is noteworthy among those observed for all of the priority municipalities that had TCPs and specialized PCCs.[16] Five screenings were performed in prisons, and one was performed at a military barracks. Those screenings were performed either in an attempt to identify contacts of tuberculosis patients or in order to provide technical training. There were no records of screenings in other vulnerable populations, such as health care students/workers, rheumatology patients, and transplant recipients. The reasons given/observed for not performing TSTs more often were the lack of a TST protocol, the low credibility of the TST, failure to request the annual TST recommended for HIV-infected individuals, and a lack of awareness that patients with latent tuberculosis should be treated.

Discussion

Although the municipalities under study are priority municipalities for tuberculosis control measures, the TCPs had operational difficulties regarding human resources, materials, and record keeping. The operational difficulties of the TCPs and STD/AIDS Programs were the underuse of TSTs, the insufficient number of professionals trained in TST administration, the lack of specialists qualified to read TST results, the lack of standardization of the syringes used, the lack of recording of the number of tests performed, and the lack of information regarding the treatment for latent tuberculosis. In numerous countries, those same operational difficulties have been reported, not only for the performance of the TST but also for pharmacological treatment.[15,17] It is estimated that, worldwide, only 1.3% of the vulnerable population received prophylaxis against tuberculosis in 2009. However, between 2002 and 2009, the number of countries providing such prophylaxis gradually increased—from 8 to 102.[1]

In 2009, the specialized Brazilian National STD/AIDS and Viral Hepatitis Program PCCs were surveyed with the *Sistema de Controle Logístico de Medicamentos* (SICLOM, Logistic Medication Monitoring System), with the objective of monitoring the number of patients being treated for latent tuberculosis. To the antiretroviral therapy request form, a field was added in which TST results and the therapeutic approach can be registered. Although 21 Brazilian states reported (to the Brazilian National Ministry of Health)

that TSTs had been performed at the specialized PCCs during the study period, only 7,972 TSTs were reportedly performed, and those tests resulted in only 539 patients being treated for latent tuberculosis (Chart 2). In the state of Mato Grosso do Sul, 148 TSTs were reported to have been administered to individuals registered in the SICLOM, resulting in 21 patients being treated for latent tuberculosis. The lack of records, the failure to send information to state managers on a regular basis, and the low number of TSTs performed in vulnerable populations are evident nationwide.

It was estimated that there were 592,914 HIV-infected individuals in Brazil in 2010.[18] Of those, at least 80% (474,331 individuals) should have been tested annually. Given that the expected rate of TST positivity is 20%, 94,866 of those individuals could be candidates for latent tuberculosis treatment. However, according to the records, only 7,972 (1.68%) of those 474,331 individuals were tested and only 573 (0.12% of the target population; 7.19% of those tested) were treated for latent tuberculosis.

Our analysis of TST use reveals a disconnect between guidelines and practice. Although scientific evidence of the importance of the TST and preventive treatment for latent tuberculosis has been collected for 18 years, this does not seem to be reflected in the number of TSTs performed in the various at-risk populations, in which the test should be administered on an annual basis, or in the number of individuals treated for latent tuberculosis.[15]

The international recommendations for TST use in vulnerable populations date from 1965, and, in 1993, the Union Against Tuberculosis and Lung Disease, together with the World Health Organization, strongly recommended that the TST be performed in such populations and that

Chart 2 - Number of tuberculin skin tests performed and number of patients treated for latent tuberculosis among HIV-infected individuals at specialized primary care clinics, by state. State of Mato Grosso do Sul, Brazil, 2009.

States	Tuberculin skin tests	HIV-infected population	Individuals treated for latent tuberculosis
	n	n	n
Rio de Janeiro	1,296	81,606	236
São Paulo	2,563	212,071	139
Paraná	2,019	28,376	44
Minas Gerais	490	41,791	37
Rio Grande do Sul	492	58,495	30
Mato Grosso do Sul	148	6,700	29
Santa Catarina	616	28,727	24
Espírito Santo	84	8,682	10
Alagoas	15	3,842	6
Tocantins	88	1,303	6
Mato Grosso	37	7,615	4
Federal District of Brasília	13	7,824	2
Acre	1	570	1
Bahia	67	17,886	1
Pará	8	10,763	1
Paraíba	1	4,773	1
Piauí	9	3,660	1
Rondônia	17	2,734	1
Amapá	1	979	0
Ceará	3	12,062	0
Maranhão	1	7,867	0
Total	7,972	548,326	573

Data registered in the Logistic Medication Monitoring System, the Brazilian National Mortality Database, and the Brazilian National CD4+/CD8+ T Lymphocyte Count and Viral Load Network Laboratory Test Control System (Brazilian Ministry of Health. Department of Health Surveillance. Department of Sexually Transmitted Diseases/AIDS and Viral Hepatitis, unpublished data, 2011).[18]

individuals with latent tuberculosis be treated.[1] That recommendation was reiterated in 1998 and 2004.[1,8,15,16] Since 1997, the Centers for Disease Control and Prevention have recommended that HIV-infected individuals undergo the TST and receive preventive treatment with isoniazid.[19]

Operational studies conducted in various Brazilian states revealed that the lack of organization at PCCs can have a negative effect on access to diagnosis and time to diagnosis, as well as on adherence to treatment and continuity of enrollment in TCPs.[20,21] The lack of standardization of syringes for the TST impedes the proper administration of the test, because the dose administered is not precisely the recommended dose, and this can increase the number of false-negative test results.[22]

It is estimated that 50% of PPD is lost because it goes out of date while still in the flask or spoils after the flask is opened; however, this loss can be reduced by the use of tuberculin syringes and by the correct handling of the product by trained professionals. The fact that few TSTs are requested contributes to PPD loss due to expiration, contamination, or flasks that remain open for more than 30 days, all of which result in loss of potency and, consequently, increase the number of false-negative results. It is known that the size of the PPD flask influences TST results because of PPD adsorption to the flask wall as a result of the ratio between PPD volume and the inner surface of the flask; therefore, flasks of lower volume might cause lower induration than that obtained when PPD is stored in larger flasks, as demonstrated in a study comparing 1.5-mL and 5-mL flasks.[23] In 2009, the Brazilian National Ministry of Health began to distribute PPD in 1.5-mL flasks.

The operational difficulties involved in performing TSTs on weekends and the lack of a strategy to counter loss to follow-up (reading) at the specialized PCCs might be factors that reduce the efficacy of TST use. The ratio between the number of patients with latent tuberculosis infection and the number of patients treated for latent tuberculosis should be calculated and used as an indicator, which might lead to a reorganization of the PCCs in an attempt to increase TST use.[6]

Our survey revealed two successful experiences during the study period: one at a specialized PCC; and the other related to a TCP through which an indigenous population was treated—that of the Mato Grosso do Sul State *Distritos Sanitários Especiais Indígenas da Secretaria Especial de Saúde Indígena* (DSEI/SESAI, Health Districts of the Special Department of Indigenous Health). At the specialized PCC, the proportion of TSTs requested was low in 2008 (19.27%). However, 109 HIV-infected individuals underwent TSTs at that PCC in 2009. On the day of sample collection for viral load determination and CD4/CD8 cell counts, those individuals also underwent the TST. Among those patients, the prevalence of latent tuberculosis was found to be 13.9%.[11] In the DSEI/SESAI, the TST coverage was high, as was that of latent tuberculosis treatment, both of which were provided at a rate far greater than that observed in the general population. In the TCP of the DSEI/SESAI, the operational aspects were well managed, as they were at the abovementioned PCC. There were strategies to counter loss to follow-up (reading), and the availability of drugs for preventive treatment was guaranteed. The information was systematized in specifically designed registries.

It is of note that, in the state capital, the decentralization of services to PCCs did not seem to increase TST use and might have resulted in disorganization at the referral centers. The TSTs performed via the TCPs should be decentralized first to referral centers (where HIV-infected individuals, transplant recipients, patients with chronic kidney disease, and patients with rheumatic diseases are treated) and subsequently to PCCs, where the demand tends to be lower.

In order to change the focus of the existing policies and develop new ones, with the objective of reducing costs, improving compliance with the operational strategies, and reducing the duplication of efforts, the definition of priority municipalities for tuberculosis control should also include cases of HIV infection or AIDS.[6] Otherwise, there is a risk that the situation observed in the present study will persist.

It takes time, formal training, and experience for professionals administering and reading TSTs to do it properly. These requirements, together with the low number of TSTs performed at PCCs, can explain why most professionals are not qualified to perform TSTs. The expansion of the public health care system led to an increase in the number of professionals hired, a reduction in the number of training courses offered, and a

substantial reduction in the number of trained professionals employed by the public health care system. Training courses should be offered annually, with the objective of developing human resources that are qualified to read TST results.[18,22,24-26]

Although studies conducted in Brazil and abroad found considerable evidence to support the recommendation that health care students and workers be screened for latent tuberculosis (at admission/hiring and annually), our survey found that this screening has not been performed, which makes it impossible to treat this at-risk population prophylactically.[11,14,27] Health care workers in the state of Mato Grosso do Sul were screened by the TST only once, in 2004, and the prevalence of latent tuberculosis was found to be 37.8%. However, the screening did not result in annual follow-up evaluations or in preventive treatment in cases of TST conversion.[10]

The integration between the STD/AIDS programs and the TCPs is limited, which constitutes an operational barrier.[15] It is recommended that TCPs be promptly integrated with other referral centers at which TSTs are performed in order to identify latent tuberculosis in adult contacts of tuberculosis patients, in individuals using TNF-α inhibitors, and in transplant recipients under immunosuppressive therapy or using corticosteroids.[7]

In the literature,[1,16,20] the reasons described for not screening individuals by the TST, as well as those described for not treating individuals with latent tuberculosis, are similar to those found in the present study: minimal physician experience in the management of preventive therapy; the fact that the benefits of preventive therapy are not made clear; the lack of credibility of the TST; and the low number of trained professionals, which is due to high staff turnover. Other factors that can be considered operational barriers are the difficulty that patients have in understanding the use of preventive treatment and the low socioeconomic status of patients, both of which result in treatment noncompliance.[16,20]

Few TSTs are performed via the TCPs and specialized PCCs that provide treatment to individuals with tuberculosis and HIV-infected individuals, and few individuals belonging to other priority groups for tuberculosis control receive treatment for latent tuberculosis. Joint activities of the Brazilian National Tuberculosis Control Program and the Brazilian National STD/AIDS and Viral Hepatitis Program can effectively reduce the number of tuberculosis cases in the long term. The public health care system should be reorganized in order to guarantee the efficient flow of information within its hierarchy. This will increase the number of TSTs performed and the number of patients treated for latent tuberculosis.

The TST remains a valuable method for controlling tuberculosis. Operational studies should be conducted in all Brazilian states in order evaluate the obstacles to TST use in the diagnosis and treatment of tuberculosis.

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