Original Article

Noncompliance with tuberculosis treatment involving self administration of treatment or the directly observed therapy, short-course strategy in a tuberculosis control program in the city of Carapicuíba, Brazil*

Abandono do tratamento de tuberculose utilizando-se as estratégias tratamento auto-administrado ou tratamento supervisionado no Programa Municipal de Carapicuíba, São Paulo, Brasil

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Abstract

Objective: To determine treatment noncompliance rates among patients participating in a municipal tuberculosis control program and to identify the variables related to noncompliance depending on the type of treatment strategy used. **Methods:** A longitudinal non-concurrent cohort study was carried out involving two cohorts of patients participating in the Tuberculosis Control Program of the city of Carapicuíba, Brazil. The first cohort comprised 173 patients with tuberculosis treated from January 1, 2003 to December 31, 2003 using self administration of treatment, and the second comprised 187 patients with tuberculosis treated from July 1, 2004 to June 30, 2005 using the directly observed therapy, short-course strategy. **Results:** Noncompliance rates decreased from 13.3% (self administration of treatment) to 5.9% (directly observed therapy, short-course), a significant difference ($p < 0.05$). For the self administration of treatment strategy, the variables significantly associated with treatment noncompliance were as follows: being an unregistered worker (relative risk [RR] = 3.06); retreatment (RR = 2.73); alcoholism (RR = 3.10); and no investigation of contacts (RR = 8.94). For the directly observed therapy, short-course strategy, no variables were significantly associated with noncompliance. **Conclusion:** The directly observed therapy, short-course strategy decreased noncompliance rates and produced better treatment outcomes, even when the risk factors for noncompliance were the same.

Keywords: Tuberculosis; Self administration; Directly observed therapy; Treatment refusal.

Resumo

Objetivo: Verificar as taxas de abandono e identificar as variáveis relacionadas ao abandono do tratamento, segundo o tipo de estratégia utilizada em pacientes matriculados no Programa de Controle da Tuberculose do município de Carapicuíba (SP) Brasil. **Método:** Estudo longitudinal não concorrente de duas coortes de tratamento de tuberculose, a primeira de 1 de janeiro a 31 de dezembro de 2003 com a estratégia tratamento auto-administrado (173 casos) e a segunda de 1 de julho de 2004 a 30 de junho de 2005 com a estratégia tratamento supervisionado (187 casos). **Resultados:** A taxa de abandono diminuiu significativamente ($p < 0,05$), de 13,3% (tratamento auto-administrado) para 5,9% (tratamento supervisionado). Na estratégia tratamento auto-administrado, as variáveis associadas significativamente ao abandono foram: estar trabalhando na informalidade (risco relativo [RR] = 3,06); ser caso de retratamento (RR = 2,73); ser alcoolista (RR = 3,10); e não ter os contatos examinados (RR = 8,94). Não houve variável associada ao abandono para os casos sob a estratégia tratamento supervisionado. **Conclusão:** A estratégia tratamento supervisionado reduziu a taxa de abandono e produziu bons resultados quanto ao desfecho do tratamento, mesmo nos pacientes com fatores de risco para abandono como na coorte tratamento auto-administrado.

Descritores: Tuberculose; Auto-administração; Terapia diretamente observada; Recusa do paciente ao tratamento.

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Introduction

Tuberculosis (TB) is an infectious disease with social and demographic features. In large urban centers, where population density is high, TB is more prevalent and is more frequently associated with social indicators of poverty, such as social exclusion, low educational level, poor housing, malnutrition, difficulties in accessing health care facilities, alcoholism and concomitant diseases, such as infection with HIV.[1-4]

After 1979, Brazil became one of the pioneer countries in the treatment of TB by means of a public health care program using a short-term (six-month) regimen designated regimen I.[1,4-6]

Due to the high efficacy of regimen I, it is possible to rapidly reduce the transmission of TB and, consequently, its incidence. Although the Brazilian Unified Health Care System provides free medication for TB nationwide, noncompliance with the treatment is the greatest obstacle to TB control and cure.[5-8]

The World Health Organization (WHO) recommends that noncompliance rates of TB programs be lower than 5%. In 2003, the mean noncompliance rate was 12% and 10.3% in Brazil and in the state of São Paulo, respectively. However, there were huge regional differences, ranging from 6.4% in João Pessoa to 18.7% in Porto Alegre. In 2004, noncompliance rates were 12.4 and 8.2% in the cities of São Paulo and Carapicuíba, respectively.[9-11]

As a worldwide strategy to avoid noncompliance and to stimulate the proper use of medication, the WHO proposed the directly observed therapy, short-course (DOTS) strategy, which is a set of political and administrative strategies, including supervised treatment in order to stimulate compliance with the treatment. This is considered one of the best forms of intervention in terms of the cost-benefit ratio.[10-13]

Currently, approximately 50% of TB patients in Brazil are being treated using the DOTS strategy. In 2004, 42.6% of all TB patients in the state of São Paulo and 23.2% of all new TB cases in the city of São Paulo were treated using this strategy.[11,13,14]

In 2004, the Carapicuíba City Council made an agreement with the São Paulo State Department of Health and the United States Agency for International Development in order to implement the DOTS strategy for all TB cases in the city. After various studies and the training of the municipal health care staff, DOTS was implemented in June 2004.

The objective of this study was to determine treatment noncompliance rates and the variables related to noncompliance of patients with TB participating in the Tuberculosis Control Program (TCP) of the City of Carapicuíba, comparing those using DOTS with those using self administration of treatment (SAT).

Methods

A longitudinal non-concurrent cohort study was carried out involving two cohorts of reported cases of TB that were fully treated (for 6 months) in the Local Health Care System of the city of Carapicuíba, in the greater metropolitan area of São Paulo. Cohort 1 consisted of patients who began treatment between January 1, 2003 and December 31, 2003 using the SAT strategy. Cohort 2 consisted of patients who began treatment between July 1, 2004 and June 30, 2005 after the implementation of the DOTS strategy in the city.

Patients residing in the city and diagnosed with TB in accordance with the Technical Guidebook for TB Control, in which the use of regimen I or regimen IR (retreatment) is recommended, were included in the study.[15]

Patients presenting drug or multidrug resistance to regimens I and IR, patients diagnosed with tuberculous meningoencephalitis and confirmed cases of relocation were excluded from the study. Cases of drug or multidrug resistance were excluded because they require treatment regimens other than regimens I or IR, and the duration of the treatment is longer than six months. For the same reason, cases of tuberculous meningoencephalitis and confirmed cases of relocation were also excluded due to the fact that treatment would be carried out in another health care facility.[15]

Table 1 - Distribution of cases of noncompliance with tuberculosis treatment by the type of strategy employed.

Type of treatment	Noncompliance n (%)	Compliance n (%)	p	RR
SAT	23 (67.6)	150 (46.0)		
DOTS	11 (32.4)	176 (54.0)		
Total	34 (100.0)	326 (100.0)	0.012	2.26

Source: Tuberculosis Control Program of the City of Carapicuíba (2003-2005). SAT: self administration of treatment; DOTS: directly observed therapy, short-course; and RR: relative risk.

Noncompliance with the treatment was defined as when patients with TB, 30 days after treatment initiation, missed the follow-up appointment and could not be reached, by means of notification or home visit, or when the administration of the medication was interrupted for more than 30 consecutive days.[15]

Data regarding the cases of TB were obtained from reporting and follow-up forms, available in the computerized database of Carapicuíba, as well as from the medical charts of patients treated in the Municipal Health Care System.

Whenever necessary, we referred to the Registry of TB Cases and Monitoring of their Treatment, standardized and regulated by the Ministry of Health, or to the Registry of Symptomatic Respiratory Cases Treated in Health Care Facilities, standardized and regulated by the Tuberculosis Control Division of the São Paulo State Department of Health Professor Alexandre Vranjac Center for Epidemiological Surveillance.

The following variables were studied: age; gender; level of education; occupation; type of case (new or retreatment); clinical form of the disease

Table 2 - Distribution of patients with tuberculosis using the self administration of treatment strategy by noncompliance/compliance, according to sociodemographic variables and general aspects of the disease.

Variables	SAT		(p)
	Noncompliance	Compliance	
	n (%)	n (%)	
Age			
0-20 years	02 (1.2)	16 (9.1)	
21-45 years	19 (11.0)	92 (53.2)	
≥46 years	02 (1.2)	42 (24.3)	0.111
Gender			
Male	18 (10.4)	88 (50.9)	
Female	05 (2.9)	62 (35.8)	0.062
Level of education			
<8 years of schooling	15 (8.8)	96 (56.5)	
≥8 years of schooling	07 (4.1)	52 (30.6)	0.481
Occupation			
Homemaker/student	04 (2.4)	39 (22.8)	
Registered employee	07 (4.1)	76 (44.4)	
Unregistered employee	12 (7.0)	33 (19.3)	0.010
Type of case			
New	14 (8.1)	126 (72.8)	
Retreatment	09 (5.3)	24 (13.8)	0.013
Clinical form			
Pulmonary	20 (11.6)	128 (74.0)	
Extrapulmonary	03 (1.7)	22 (12.7)	0.567
Active tuberculosis			
Yes	13 (8.8)	97 (65.5)	
No	07 (4.8)	31 (20.9)	0.222
Duration of signs/symptoms			
<8 weeks	07 (4.1)	61 (35.3)	
≥8 weeks	16 (9.2)	89 (51.4)	0.242
Investigation of contacts			
Yes	01 (0.7)	49 (31.0)	
No	17 (10.7)	91 (57.6)	0.007

Source: Tuberculosis Epidemiology database, Tuberculosis Control Program - Carapicuíba (2003-2005). SAT: self administration of treatment.

Table 3 - Distribution of patients with tuberculosis using the self administration of treatment strategy by noncompliance/compliance, according to hospitalizations and concomitant diseases.

Variables	SAT		(p)
	Noncompliance	Compliance	
	n (%)	n (%)	
Hospitalization			
Yes	02 (1.2)	13 (7.5)	
No	21 (12.1)	137 (79.2)	0.623
Concomitant diseases			
Yes	12 (19.7)	49 (80.3)	
No	11 (9.8)	101 (90.2)	0.058
HIV coinfection			
Yes	03 (1.7)	06 (3.4)	
No	20 (11.7)	144 (83.2)	0.101
Diabetes			
Yes	03 (1.7)	13 (7.5)	
No	20 (11.6)	137 (79.2)	0.359
Alcoholism			
Yes	07 (4.2)	16 (9.2)	
No	16 (9.2)	134 (77.4)	0.017
Mental diseases			
Yes	01 (0.6)	01 (0.6)	
No	22 (12.7)	149 (86.1)	0.249
Hypertension			
Yes	0 (0.0)	3 (1.7)	
No	23 (13.3)	147 (85.0)	0.650
Other diseases			
Yes	00 (0.0)	15 (8.7)	
No	23 (13.3)	135 (78.0)	0.106

Source: Tuberculosis Epidemiology database, Tuberculosis Control Program - Carapicuíba (2003-2005). SAT: self administration of treatment.

(pulmonary or extrapulmonary); active pulmonary TB (positive sputum smear microscopy); duration of signs/symptoms prior to diagnosis (in weeks); investigation of contacts; hospitalizations due to TB; and concomitant diseases.

For data collection, individual standardized forms were created. These forms were then encoded and entered into a specific database using a statistical software package (Epi Info 2000, version 3.3). Data were entered in duplicate and the Epi Info 'Validate' tool was used in order to check data consistency and eliminate typographical errors.

Descriptive analysis for the principal variables was carried out, as were measurements of central tendency for quantitative variables.

In order to identify variables related to noncompliance (bivariate analysis), the dependent variable was dichotomized between 'yes' or 'no,' regarding unfavorable outcome (noncompliance with the treatment) in the two cohorts (SAT and DOTS).

In order to determine this association, we calculated the relative risk (RR). The chi-square test or Fisher's exact test were used when indicated. The level of significance was set at 5%. Confidence intervals were unnecessary, since sampling was not used in the study.

The present study was approved by the Ethics in Research Committee of the Federal University of São Paulo.

Results

During the study period, 360 cases of TB met the eligibility criteria. Cohort 1 (SAT) comprised 173 cases and cohort 2 (DOTS) comprised 187 cases.

From the final analysis, 39 cases were excluded: 23 (59%) cases due to confirmed relocation; 9 (23.1%) due to drug or multidrug resistance; 4 (10.2%) because the patients resided in other cities; and 3 (7.7%) because the patients were diagnosed with tuberculous meningoencephalitis.

Of the cases included, 218 (60.6%) were in males and 142 (39.4%) were in females, a ratio of approximately 1.5:1. This ratio was the same in both cohorts. The mean age of the patients using SAT was 37.6 years (median, 38 years), compared with 37.1 years (median, 38 years) for those using DOTS. There was no statistical difference between the two cohorts regarding age.

Of the 53 cases of retreatment using SAT or DOTS, 42 (79.2%) restarted treatment due to previous noncompliance, and 11 (20.8%) restarted treatment due to recurrence of TB.

The most common clinical form of TB was the pulmonary form (83.6%). Among the extrapulmonary manifestations, the diagnoses were pleural TB in 35 (59.3%) patients, peripheral lymph node TB in 10 (16.9%), miliary TB in 3 (5.1%), osseous TB in 2 (3.4%) and TB in other locations in 9 (15.3%).

The mean duration of signs and symptoms among the patients using SAT was 13 weeks, compared with 10 weeks among those using DOTS (median,

8 weeks for both cohorts). Of the 360 patients evaluated, 32 (8.9%) were hospitalized, primarily for 'diagnostic confirmation', as was the case for 18 (56.1%). The second most common reason for hospitalization, found for 9 (15.8%) of the patients, was respiratory insufficiency. The mean length of hospitalization was 14 days.

The most prevalent concomitant diseases in both cohorts were alcoholism (in 15%) and diabetes mellitus (8.9%). The prevalence of HIV coinfection was 5.2% for those using SAT and 4.8% for those using DOTS, with no statistical difference.

Table 1 shows that noncompliant cases were significantly more common in the SAT group than in the DOTS group. The risk of noncompliance with TB treatment was approximately 2.3-times higher for the patients using SAT than for those using DOTS.

Tables 2 and 3 show the variables possibly related to noncompliance of the patients using SAT. Being an unregistered worker (RR = 3.06), retreatment (RR = 2.73), no investigation of contacts (RR = 8.94), and alcoholism (RR = 3.10) significantly contributed to noncompliance with the treatment among the patients using SAT.

Table 4 - Distribution of patients with tuberculosis using the directly observed therapy, short-course strategy by noncompliance/compliance, according to sociodemographic variables and general aspects of the disease.

Variables	DOTS		(p)
	Noncompliance	Compliance	
	n (%)	n (%)	
Age			
0-20 years	03 (1.6)	23 (12.3)	
21-45 years	06 (3.2)	102 (54.5)	
≥46 years	02 (1.1)	51 (27.3)	0.377
Gender			
Male	06 (3.2)	106 (56.7)	
Female	05 (2.7)	70 (37.4)	0.470
Level of education			
<8 years of schooling	07 (3.9)	105 (58.3)	
≥8 years of schooling	04 (2.2)	64 (35.6)	0.596
Occupation			
Homemaker/student	02 (1.4)	50 (27.4)	
Registered employee	07 (3.8)	70 (38.5)	
Unregistered employee	02 (1.4)	51 (27.5)	0.336
Type of case			
New	08 (4.3)	159 (85.0)	
Retreatment	03 (1.5)	17 (9.2)	0.099
Clinical form			
Pulmonary	10 (5.3)	143 (76.5)	
Extrapulmonary	01 (0.6)	33 (17.6)	0.354
Active tuberculosis			
Yes	07 (4.6)	94 (61.8)	
No	03 (2.0)	48 (31.6)	0.553
Period of signs/symptoms			
<8 weeks	04 (2.3)	88 (47.0)	
≥8 weeks	07 (3.7)	88 (47.0)	0.287
Investigation of contacts			
Yes	05 (3.1)	107 (64.4)	
No	05 (3.1)	49 (29.4)	0.190

Source: Tuberculosis Epidemiology database, Tuberculosis Control Program - Carapicuíba (2003-2005). DOTS: directly observed therapy, short-course.

Table 5 - Distribution of patients with tuberculosis using the directly observed therapy, short-course strategy by noncompliance/compliance, according to hospitalizations and concomitant diseases.

Variables	DOTS		(p)
	Noncompliance	Compliance	
	n (%)	n (%)	
Hospitalization			
Yes	00 (0.0)	42 (22.4)	
No	11 (6.0)	134 (71.6)	0.056
Concomitant diseases			
Yes	04 (5.7)	66 (94.3)	
No	07 (6.0)	110 (94.0)	0.605
HIV coinfection			
Yes	00 (0.0)	09 (4.8)	
No	11 (5.9)	167 (89.3)	0.572
Diabetes			
Yes	00 (0.0)	16 (8.5)	
No	11 (5.9)	160 (85.6)	0.363
Alcoholism			
Yes	03 (1.6)	28 (15.0)	
No	08 (4.3)	148 (79.1)	0.267
Mental diseases			
Yes	00 (0.0)	04 (2.1)	
No	11 (5.9)	172 (92.0)	0.783
Hypertension			
Yes	0 (0.0)	08 (4.2)	
No	11 (5.9)	168 (89.9)	0.610
Other diseases			
Yes	02 (1.1)	13 (6.9)	
No	09 (4.8)	163 (87.2)	0.217

Source: Tuberculosis Epidemiology database, Tuberculosis Control Program - Carapicuíba (2003-2005).DOTS: directly observed therapy, short-course.

Tables 4 and 5 show that there was no significant association between those same variables and noncompliance with the treatment among the patients using DOTS.

Discussion

In the present longitudinal study, two nonconcurrent cohorts were compared, according to the treatment/strategy used: SAT or DOTS. In Carapicuíba, the implementation of DOTS, a strategy supported by the literature, recommended by WHO for developing countries and encouraged by the Ministry of Health, has made randomization impossible and unnecessary in the simultaneous comparison between the two strategies, since DOTS has shown a better cost-benefit ratio in various studies in the literature.[11,13]

Our results show that noncompliance rates were significantly lower among patients using DOTS than among those using SAT, almost reaching the target rate of 5% recommended by the Brazilian National TCP and the WHO. As previously mentioned, the risk of noncompliance was 2.3-times higher for those using SAT than for those using DOTS. These data indicate that the Carapicuíba TCP benefited from the implementation of DOTS and corroborate the results of other studies.[3,10,16]

To ensure the regularity of the administration of medication and to maintain treatment throughout the recommended period have been the critical points for the success of standardized therapeutic regimens for TB and the control of the chain of transmission. Strategies such as DOTS or other possible adapted variations, depending on the local characteristics, particularities and conditions, should be developed and improved, based on the promising results of DOTS and other programs for the control of TB.[5,9,11,16,17]

Most of the patients studied were from 21 to 45 years of age, which is considered to be the most economically productive age bracket, and males predominated, as did a low level of education, although none of these sociodemographic variables presented a significant association with noncompliance in either of the cohorts studied. However, being an unregistered worker, typically with a low salary and having had little education, was associated with noncompliance in the cohort using the SAT strategy, a finding that is in agreement with those of other studies.[7,8,18-20]

Some studies have shown that being in retreatment (due to noncompliance or recurrence) is strongly associated with noncompliance. This association was also found in the present study for the cases using SAT,[8,17] but not for those using DOTS.

Alcoholism was the most highly prevalent comorbidity in the present study and was significantly associated with noncompliance among TB cases using SAT. In addition, studies in the literature have shown that alcoholism is an significant risk factor for poor prognosis and unfavorable outcome in the treatment of TB.[7,20-23]

Another significant aspect regarding noncompliant patients using SAT was the fact that, when fewer contacts were investigated, the rates of noncompliance with the treatment were higher. Therefore, social and family support is presumed to have a positive influence on treatment outcomes.[8,18,23]

Knowledge of the disease and the demystification of beliefs regarding its treatment are significant factors for compliance, and the health care staff should monitor the participation of the family throughout the treatment. In addition, the patient is not the only individual to be affected by the disease.[24]

After the implementation of DOTS and the resulting decrease in noncompliance rates, no association between noncompliant patients using DOTS and any of the variables studied was found, which might be attributable to the lower number of noncompliant patients. In general, the lower noncompliance rate among patients using DOTS might be related to the more intimate, frequent and humanized contact between patients and the entire health care staff, resulting in a stronger bond between patients, their companions, families and the health care facility, as well as in better compliance with the therapeutic regimen and more favorable treatment outcomes, although the political administrative infrastructure as a whole also plays a role in improving the performance of the TCP.[8,11,14,17,19,25]

Political, administrative, organizational and social changes, involving health care centers, the community, families and the media, are necessary. Ultimately, health care professionals should be trained and sensitized, by means of training courses and continuing education regarding DOTS. These will promote the more efficacious performance of TB control programs.

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