ORIGINAL ARTICLE

Association of outcomes with comprehension, adherence and behavioral characteristics of tuberculosis patients using fixed-dose combination therapy in Contagem, Minas Gerais, Brazil

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ABSTRACT

The present study aimed to assess the association of outcomes with comprehension, adherence and behavioral characteristics of tuberculosis (TB) patients using fixed-dose combination (FDC) therapy in the city of Contagem, MG, Brazil. This study used standardized questionnaires to collect data. Outcomes included cure in 77.2% (64/ 83), noncompliance with treatment in 20.4% (17/ 83), and absence of organ failure or death cases. The rate of adherence to treatment was high (71.1% - 59/ 83), while the level of comprehension of the treatment was insufficient for the majority of patients (72.3% - 60/ 83). When a greater number of medicines was used, the chance of noncompliance with treatment increased exponentially (p = 0.00 - OR 1.72). Light-skinned black patients, alcoholics and those who live with HIV/ AIDS showed a significant association with noncompliance with treatment (p=0.039 - OR 3.38, p=0.002 - OR 4.68, and p=0.001 - OR 9.68, respectively). Comprehension also presented a significant association with noncompliance with treatment (p=0.01 and OR 5.76 and CI 1.49-22.29). The probability of noncompliance with treatment in the first few months was greater than in the subsequent months. This study demonstrates that if the TB patients had a better understanding of the treatment, the outcome would have been more favorable as regards a proper cure.

KEYWORDS: Tuberculosis. Antibacterials. Comprehension.

INTRODUCTION

Tuberculosis (TB), considered a public health issue in its pulmonary clinical form, has been identified as the commonest form of new cases of the disease[1]. To confront this disease, one of the most important factors is an effective treatment. For this reason, Brazil has adopted procedures that aim to increase patients' adherence and reduce patients' noncompliance with treatment, thus increasing the cure rate of the disease[2].

Patient noncompliance with TB treatment is a troublesome scenario and requires strategic measures to maintain a higher adherence to treatment[3]. Therefore, the success of the treatment depends heavily upon the proper embracement and follow-up of the patients by healthcare professionals[4].

The knowledge or comprehension of the disease is of great importance in treatment adherence. Adverse reactions to medications, the treatment regimen, as well as treatment costs for patients and their families can influence the outcome leading to a higher noncompliance[4,5,6].

In 2009, the National Program for the Control of Tuberculosis (NPCT), introduced ethambutol as the fourth drug in the first stage of the basic therapy. Ethambutol was added due to the increase in primary resistance to H[4]. There was a change in the pharmacological presentation of the schema, which began with FDC tablets containing four drugs - Rifampicin, Isoniazid, Pyrazinamide, and Ethambutol (RHZE) in the intensive stage[2,8]. The World Health Organization (WHO) also recommends the use of FDC to increase TB treatment adherence[9,10].

The present study aimed to assess the association of outcomes with comprehension, adherence and behavioral characteristics of tuberculosis (TB) patients using FDC therapy in the city of Contagem, MG, Brazil.

METHODS

This study was a prospective cohort aimed at evaluating the outcome of anti-TB treatment after the application of the new FDC (RHZE/ RH) drug therapy, conducted in Contagem, MG, Brazil. This study consisted of patients who were 18 years of age or older, with pulmonary or extra pulmonary TB, followed up at a primary care unit from November 2013 to April 2015, and defined as new cases. These patients were selected by the results registered in the TB laboratory information system or when they received the medicament to treat tuberculosis for the first time in regional pharmacies.

Patients submitted to retreatment outside the Primary Healthcare Unit (PHU) of Contagem, who died before the interview, were treated in other cities, and did not complete the treatment before the end of the study were excluded from this study.

The explanatory variables were collected by means of direct interviews conducted by the researcher using a standardized questionnaire. These variables included sociodemographic parameters (gender, age, education level) and socioeconomic characteristics (income); behavioral characteristics: use of illegal drugs; clinical characteristics (comorbidity); and Directly Observed Treatments (DOTS). To assess alcoholism, the CAGE (Cutdown, Annoyedby Criticism, Guilty and Eye-opener) questionnaire was applied[11].

Morisky scale of adherence to treatment was adapted to assess the adherence of patients to TB treatment, which uses eight questions with "Yes" or "No" answers. A total score of eight is considered high adherence, a score of less than eight but higher than six is considered average adherence, and a score below six is considered low adherence[12]. This questionnaire, aimed at assessing comprehension, was adapted for TB, and the instrument used to assess the

comprehension of treatment considers the answers sufficient when patients obtain 70% or more points and insufficient when the score is less than 70%[5,13]. This instrument was not applied to assess the comprehension of the use of other medicines, only to quantify them. This questionnaire was adapted from CIPOLLE to obtain the following variables: marital status, residency, smoking habits and side effects related to the drugs.[14] All of the instruments were applied in three interviews during the patient's treatment, the first one being conducted at the end of the first month, the second one at the end of the second month, and the third one at the end of the sixth month.

The outcomes considered in this study included: cure, noncompliance with treatment, failure or death after the interview[7,15].

The descriptive analysis with the frequency distribution was conducted with categorical variables. For continuous variables, the evaluation of the core and dispersion tendencies (median, average and standard deviation) were assessed using the Statistics Analysis Package, STATA 12.1. The magnitude of the association was estimated by means of the odds ratio (OR). For all of the analyses the significance level was $p \leq 0.05$, with a confidence interval (CI) of 95%.

A logistic regression analysis was conducted in two stages. The first stage was a selection of the explicative variables with potential of association between each variable and the outcome. The first stage was done using a logistic regression with three variables, the outcome, the explicative variable tested and the moment at which there was noncompliance with the treatment between the first and second interview. For the association study, between the outcomes and the explanatory variables, two subjects which died before the interview were excluded, so the outcome became a dichotomic variable (cure/ noncompliance with treatment). This kind of procedure was a univariate logistic regression model controlled by moment. The variables with p-values equal to or greater than 0.20 in the Wald test, in the univariate controlled analysis, were manually selected to begin the multivariate analysis with a stepwise process, with a backward selection. The multivariate analysis was used to assess the association between the explicative variables and the outcome response variable: cure and noncompliance with treatment.

The adjustment of the Hosmer & Lemeshow model was also conducted. In this case, to demonstrate that the model was accepted, the null hypothesis should also be accepted, that is, $p > 0.05$.

This study was approved by the Research Ethics Committee from the Federal University of Minas Gerais (UFMG), under the protocol number CAAE 16298413.0.0000.5149.

RESULTS

Eighty-three (83) patients were included in this study (Figure 1), of which 59.0% (49/ 83) were male. Ages varied from 18 to 83 years, with an average age of 42.19 years (SD-15.0). The clinical form of TB was pulmonary in 84.3% (70/83) of the patients. The variables of sociodemographic, socioeconomic, behavioral and clinical characteristics, as well as those related to the drug therapy are in Table 1. Two patients were excluded because they did not complete the treatment before the end of the study.

The frequency of adherence to treatment was high (80.8% - 67/ 83). In 10.8% (9/ 83), the adherence was average, while in 8.4% (7/ 83) it was low (Table 1).

All patients presented side effects; however, the majority (97.5%) presented only a few reactions, and this variable had no effect on the patients' noncompliance with treatment (Table 1).
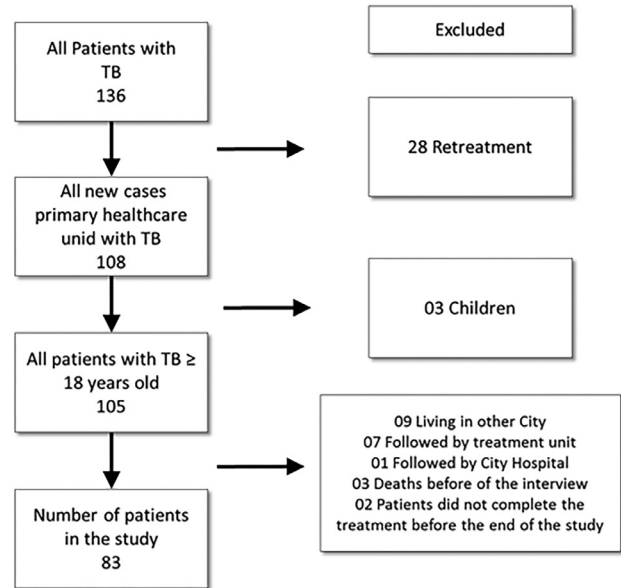
Figure 1 - Study sample

Table 1 - Descriptive analysis of the sociodemographic behavioral, clinical and pharmacotherapeutic characteristics (n = 83)

	Cured	Noncompliance	Death
	N (%)	N (%)	N (%)
SOCIODEMOGRAPHIC			
Age (> 18 years)			
18 – 41	60(72.4)	10(12.0)	0
42 – 83	4(4.8)	7(8.4)	2(2.4)
(Average 42.19)			
Gender			
Male	39(47.0)	9(10.8)	1(1.2)
Female	26(31.3)	7(8.4)	1(1.2)
Housing			
House /Apartment	63(75.9)	15(18.0)	2(2.4)
Shelter	1(1.2)	2(2.4)	0
Race			
Light-skinned black	44(53.0)	15(18.1)	2(2.4)
Other races	20(24.1)	2(2.4)	0
Income			
With Income	48(57.8)	10(12.1)	2(2.4)
Without Income	16(19.3)	7(8.4)	0
Education level			
< 08 years	48(57.8)	13(15.7)	1(1.2)
> 08 years	16(19.3)	4(4.8)	1(1.2)
CLINICAL			
Form			
Pulmonary	52(62.7)	16(19.3)	2(2.4)
Extrapulmonary	12(14.4)	1(1.2)	0
Health problems			
AIDS	5(6.0)	3(3.6)	0
Diabetes	7(8.4)	2(2.4)	0
Others	27(32.6)	5(6.0)	2(2.4)
No health problems	26(31.4)	6(7.2)	0

	Cured	Noncompliance	Death
	N (%)	N (%)	N (%)
TS/DOTS			
Yes	9(10.8)	5(6.0)	0
No	55(66.3)	12(14.5)	2(2.4)
PHARMACOTHERAPEUTIC			
Side effects			
Lesser	64(77.1)	15(18.1)	2(2.4)
Greater	0	2(2.4)	0
Non-TB Medicines			
Without use of medicines	25(30.1)	11(13.3)	0
01 medicine	13(15.7)	4(4.8)	0
02 medicines or more	24(28.9)	4(4.8)	2(2.4)
Adherence			
High	51(61.5)	14(16.9)	2(2.4)
Average	9(10.8)	0	0
Low	4(4.8)	3(3.6)	0
Understanding			
Sufficient	18(21.7)	3(3.6)	0
Insufficient	46(55.4)	14(16.9)	2(2.4)
BEHAVIORAL			
Smoking			
Yes	10(12.0)	5(6.0)	0
No	54(65.1)	12(14.5)	2(2.4)
Alcoholism			
Yes	10(12.0)	6(7.2)	0
No	54(65.1)	11(13.3)	2(2.4)
Marital status			
Single/Divorced/Widow	30(36.1)	10(12.1)	0
Married/Stable Union	34(41.0)	7(8.4)	2(2.4)

Patients presented full cure in 77.2% (64/83) of the cases and noncompliance with treatment in 20.4% (17/83). There were no cases of organ failure or death caused by TB. Death after the interview by other causes was 2.4% (2/83).

Age, gender, marital status, education level, smoking habits, having a regular income or not and supervised treatment proved to be unassociated with patients' noncompliance with treatment (Table 1).

The level of comprehension of TB treatment was insufficient for the majority of patients: 72.3% (60/83).

The use of other medications in addition to anti-TB drugs happened in 56.6% (47/83). When the patient used a large number of medications the probability of noncompliance with treatment increased exponentially (OR 1.72), with p=0.00 (Table 2).

Light-skinned black patients, alcoholics and those who live with HIV/AIDS presented a significant association with the noncompliance with TB treatment (p=0.03, p = 0.00, and p=0.00, respectively). The parameter comprehension has also presented a significant association with the noncompliance with treatment (p=0.01, OR 5.76, and CI 1.49-22.29), as shown in Table 2.

Figure 2 shows that the probability of patients' noncompliance with TB treatment in the first months is greater than in the subsequent months, and that the
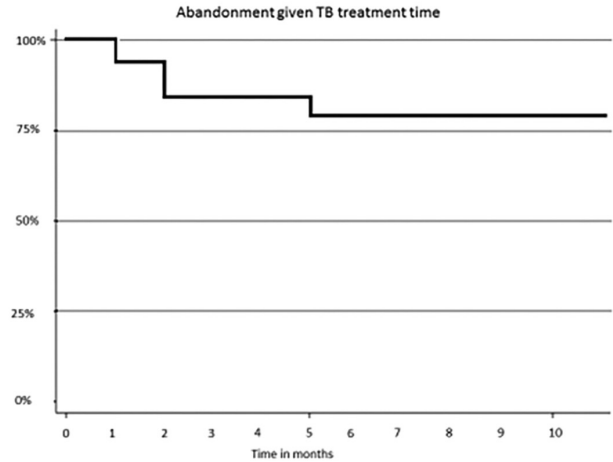

Figure 2 - Percentage of noncompliance with treatment according to the time of TB treatment

accumulated incidence was of 20.4% in the first two months. In 6.0% (5/83) of the patients who were noncompliant with the treatment, the noncompliance happened after the first interview, while in 10.8% (9/83) it happened after the second interview.

DISCUSSION

In 2003, Contagem was classified by the Brazilian

Table 2 - Multivariate analysis of sociodemographic, behavioral, clinical and pharmacotherpeutic variables (n= 83)*

Variable/category	Total n=83 (%)	OR Crude	OR Ajust	CI	P
Comprehension					
Insufficient	60 (72.30)	8.00	5.76	1.49-22.29	0.01
Sufficient	23 (27.70)				
Income					
Without income	23 (27.70)	2.1	2.08	0.88-4.93	0.09
With income	60 (72.30)				
Race					
Light-skinned black	60 (72.30)	3.40	3.38	1.06-10.77	0.03
Other races	23 (27.70)				
Smoking					
Yes	15 (18.10)	2.25	1.52	0.60-3.85	0.38
No	68 (81.90)				
Use of other non-anti-TB medicines					
No use	36 (43.37)				
01 medicine	17 (20.49)	1.63	1.72	1.44-2.06	0.00
02 medicines or more	30 (36.14)	2.78	2.94		
Alcoholism					
Yes	16 (19.30)	2.95	4.68	1.74-12.61	0.00
No	67 (80.70)				
AIDS					
Yes	8 (9.60)	2.53	9.68	2.63-35.70	0.00
No	75 (90.40)				

*The model was controlled as of the beginning of the interview.

Health Ministry (BHM) as a priority city in the number of TB cases[7]. In this city, the noncompliance with treatment is above that defined as acceptable by the WHO and the BHM, which is less than 5%[4].

This study was conducted due to the change of TB treatment for FDC in 2009, considering that studies on the impact and outcome of new cases treated with FDC are scarce in the country.

The present study found that the cure rate was greater (77.2%) when compared to data from 2008 (prior to application) (69.1%), including all clinical forms; however, it has also proved to be quite inferior to that set forth by the WHO (85% cure rate for pulmonary TB cases)[4].

Noncompliance with treatment was similar (20.4%) to the data from 2008 (19.2%). The cure rate increased due to the reduction of deaths and organ failure, yet the noncompliance with treatment remained the same. Although other studies[17,18,19] report similarities and divergences with the present study, none used primary data.

Although some sociodemographic, clinical and behavioral data in our study are not related to patients' noncompliance with treatment, other studies have shown this relationship regarding age, gender, marital status, residency, education level, having a regular income or not, DOTS and smoking habit (Table 1)[20,21,22,23]. These studies used methods or analyses of results that were different from the ones used in the present study, which may well have generated divergences. In fact, the statistical analysis used in our study assessed the results considering the variables controlled by the moment of noncompliance with treatment between the first and second interviews regarding the parameter adherence, whose association with DOTS has been previously studied and demonstrated[23,24].

FDC drug therapy is recommended by the WHO as an additional measure to increase patients' adherence to TB treatment[9,10]; however, other studies report that this formulation is not related to the noncompliance with treatment[17].

The insufficient level of comprehension presented a significant association with patients' noncompliance with treatment. Therefore, it is necessary to invest in strategies that improve the quality of the guidelines provided to the patients. It is essential to encourage the communication of healthcare professionals with patients on an individual basis so that the patient will be able to understand the guidelines and the success of treatment. Note that the patients in this study received no incentives or any orientation about the disease.

The medical advice provided by healthcare professionals concerning the medicines and their correct use must be a priority. In addition, comprehension of the difficulties and facilities that patients face to understand their treatment will help healthcare professionals to develop educational strategies aimed at the therapeutic process. The study showed that if the TB patients had understood the treatment the results could have been more favorable concerning their full cure.

Although no other studies have shown the association between the use of other medicines, other than those for TB, with patients' noncompliance with treatment, in the present study, it was evident that each added medication increased the probability of noncompliance with treatment. However, some authors report that the association of various medicines interferes with the outcome[25].

The side effects were the most commonly identified factor associated with noncompliance due to the method used in this study (interview), which shows the relevance and reliability of the information, given that the studies that reported only 20% and less side effects used secondary data and were not conducted with the entire population of a given city[17].

The risk factors associated with noncompliance with treatment such as light-skinned blacks, alcoholics and patients who live with HIV/ AIDS, illustrate that these social and clinical questions are still important in an attempt to develop medical care actions geared toward these individuals, thus leading to TB control. Other authors have also observed this relationship as a predictor of noncompliance with treatment[22].

As described by other authors[22], the present study demonstrated that the probability of patients' noncompliance with treatment, especially in the first two months, is greater, since the patient feels better, believes that he/she is cured and that there is no further need to continue taking the medicine. This reiterates the importance of the patient's comprehension of the treatment. Thus, healthcare professionals should devote more time to the process of providing medical advice to patients, as well as in the follow up to guarantee all possible medical care to the patient. It is important to remember that these professionals should create ties with their patients so that the Health Unit can become a reference for these complications[26].

The main limitation of this study was the lack of assessment of the comprehension and adherence to other medicines used to treat other medical conditions that could interfere in the results; however, this was not within the scope of this study.

It is therefore possible to conclude that the outcome of TB treatment after the application of the new FDC drug therapy in Contagem showed that the cure was below the recommended rate by WHO while noncompliance was above and that patients' comprehension was associated with their noncompliance with treatment.

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