

Assessment of the effectiveness of a home-based care program for patients coinfecting with tuberculosis and human immunodeficiency virus after discharge from a reference hospital in South-Eastern Brazil

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ABSTRACT

The effectiveness of tuberculosis treatment delivered by a home-based care program to patients coinfecting with HIV was compared with that of a service provided by outpatient departments. A retrospective study was made of a cohort of coinfecting patients discharged from hospital between January 1998 and December 2002 who had been followed-up for one year within one of these programs. Two-hundred-and-forty-three patients who met the inclusion criteria were grouped according to their treatment program (group 1 received home-based care; group 2 attended outpatient departments) and then paired one-to-one across the groups by gender, age and level of education. Only 48 patients from each group could be paired. Apart from the duration of HIV infection, there were no statistically significant differences ($P < 0.05$) between patients in the two groups with respect to social-demographic status and clinical or laboratory characteristics. In group 1, 75.0% of patients attained successful tuberculosis treatment compared with 72.9% of those in group 2 ($P = 0.816$). Treatment was abandoned by 22.9% of patients in group 1 and by 54.2% of those in group 2 ($P = 0.008$). The death rate within one year after discharge was 20.8% for group 1 compared with 6.3% for group 2 ($P = 0.334$). Although both programs achieved a similar success rate in the treatment of tuberculosis, patients receiving outpatient care were three to eight-times more likely to abandon the program. The importance of assigning patients at-risk of abandoning treatment to a home-based care program after discharge from hospital is emphasized.

Keywords: AIDS; tuberculosis; treatment outcome; adherence to treatment; home-based care.

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INTRODUCTION

Tuberculosis (TB) is one of the most important complications of HIV infection¹ and requires multi-drug therapy over an extended period. Consequently, for both infections, close adherence to the treatment regime and careful monitoring of drug resistance are critical program issues.² The successful treatment of TB requires appropriate medication as well as continuous supervision by medical staff including the direct observation of drug intake and monitoring of the disease throughout the treatment by bacteriological examination of the sputum. If all of these criteria are met, the control of TB is one of the most cost-effective health interventions.³ However, the number of TB cases is increasing worldwide, and the HIV pandemic is considered to be one of its major causes.^{4,5} In developed countries

an increase in cases was due to coinfection with HIV, and paradoxically, the increase in longevity with the emergence of TB in the elderly. These groups have accumulated and caused cohabiting institutional outbreaks. Poorer countries, on the other end, kept and maintained high incidence rates increased in most of them between past and present decades.⁶ Among the intermediate countries, some have experienced a gradual reduction in the incidence of TB, as is the case of Brazil.^{7,8} TB is known to accelerate the progression of HIV and is associated with decreased survival.⁹ Moreover, TB and HIV have a number of characteristics in common and there is a clear requirement for an evidence-based international strategy to combat both diseases.¹⁰

In Brazil, at least 100,000 individuals are coinfecting with TB/HIV. Whilst the intro-

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duction of highly active antiretroviral therapy (HAART) has resulted in a significant therapeutic breakthrough in the treatment of HIV-patients, non-adherence to the prescribed regime remains a formidable barrier to the success of the treatment,^{11,12} and innovative approaches are required in order to increase access and adherence to HAART, particularly amongst problematic sectors of the community.¹²⁻¹⁴ Since 1995, the Ministry of Health in Brazil has guaranteed the availability of HAART for all citizens suffering from AIDS by the establishment of a comprehensive national program referred to as the *Programa de Alternativas Assistenciais*.¹⁵ This program encompasses both specialized assistance service (*Serviços de Atendimento Especializado*; SAE) that is delivered by outpatient departments of hospitals, and home therapy assistance (*Assistência Domiciliar Terapêutica*; ADT), the home-based care service of which is provided by interdisciplinary teams.

Clearly, the access of HIV-patients to HAART is essential in order to reduce the incidence of HIV-related TB.¹⁶ However, very few reports have compared the effectiveness of the intervention provided by the ADT program with that of self-administered treatment supervised by SAE in the follow-up of coinfecting TB/HIV patients, especially those recently discharged from hospital.^{9,17} In order to compare the two programs, the success rate of TB treatment and the adherence to tuberculostatic and antiretroviral therapies of patients diagnosed with TB/HIV were monitored over a period of one year following their discharge from a hospital in Belo Horizonte (MG, Brazil) specializing in infectious and parasitic diseases.

METHODS

Study design

Details of the study were presented and approved by the Ethical Committee of UFMG and *Hospital Eduardo de Menezes*. A retrospective study of a cohort of HIV-diagnosed patients¹⁸ that were treated for TB in the *Hospital Eduardo de Menezes – Fundação Hospitalar do Estado de Minas Gerais* (HEM-FHEMIG) during the period from January 1st, 1998 to December 31st, 2002 was conducted using the hospital records as reference materials. Patients were followed up for one year after their discharge from hospital except when a subject abandoned the program or died during the period.

Study population

HIV-diagnosed patients were classified into two groups: group 1 consisted of patients who were followed up by the ADT program organized by HEM-FHEMIG imme-

diately after their discharge, whilst group 2 included patients who were followed up by the SAE program organized either by HEM-FHEMIG or by the *Centro de Referência e Treinamento em Doenças Infecciosas e Parasitárias Orestes Diniz* (*Prefeitura Municipal de Belo Horizonte and Hospital das Clínicas da Universidade Federal de Minas Gerais*). Within each group, all patients older than 18 years, of both gender, and living in the metropolitan area of Belo Horizonte were initially included in the study. Patients who had left the hospital against medical advice, patients who had not engaged in one of the two care programs indicated above, patients who had returned to the hospital within seven days of their formal discharge, patients who had been transferred to other medical centers, and patients who had disappeared were excluded from the study.

A total of 240 patients were initially included in the study. The 57 patients comprising group 1 had been followed up by ADT for a variable length of time, according to the protocol adopted by the team, and were eventually transferred to one of the SAE programs. Patients received weekly home visits of up to three members of an interdisciplinary team composed of physicians, nurses and aides, physical therapist, psychologist and social assistant. They earned their medications according to demand and control of use was done by counting the tablets allowing immediate assessment of adherence to therapy. A caregiver was selected and trained to give the medications and perform the care directed by the team.

The 183 patients forming group 2 had been followed up exclusively by one or both of the SAE programs. Patients in this group collected their medicines at one-to-three-monthly intervals from an outpatient department and were examined by a consultant infectious diseases specialist at that time. The type of assistance delivered to the patients after their discharge had been defined according to appropriate medical criteria during their period of hospital confinement. On this occasion, each patient had been accompanied by a relative or a community member who had accepted the responsibility of looking after them and making sure that the medications were taken as recommended by the medical team.

Selection of patients

After all of the data pertaining to the patients in the study population had been recorded, patients in group 1 were paired with those in group 2 on a one-to-one basis with respect to gender, age (± 5 years) and educational level (illiterate, primary school, secondary school or university degree). All three features should be fulfilled. Patients in group 1 who did not find perfect matches in group 2 were excluded.

Determination of treatment outcome

At the conclusion of the follow-up period, patients were classified as having (I) adhered to the treatment, (II) abandoned the treatment, or (III) died (regardless of the cause of death). Patients were deemed to have adhered to the treatment if they continued their TB medication for more than 80% of the time previously specified and failed with the antiretroviral treatment for less than 30 days. Patients who had adhered to the treatment were deemed to have received a successful TB treatment if they completed the treatment regimen and achieved clinical recovery,¹⁹ or if they attained a cure of the disease (that is, two consecutive negative bacilloscopy tests and presenting clinical recovery).

Statistical analysis

All data were recorded using appropriate standardized forms. Statistical analyses were carried out using SPSS (SPSS Inc., Chicago, IL) version 11.0 software. Descriptive and univariate analyses employing the χ^2 test and Fischer's exact test were used to detect statistically significant differences between categories. Continuous variables were tested by comparison of their mean values within a 95% confidence interval. In order to perform multiple regression univariate analysis, all variables presenting $P < 0.25$ were considered: differences were deemed significant at $P < 0.05$.

RESULTS

Of the total 240 patients, 57 were included in group 1 and 183 patients in group 2. Adherence to treatment one year after hospital discharge was achieved in 50.9% of patients in group 1 and 53% of those in group 2. The abandonment of treatment one year after hospital discharge was developed by 28.1% of patients in group 1 and 42.1% of patients in group 2 with $p = 0.129$ with a relative risk (RR) of 0.65 confidence interval (CI) 95% from 0.37 to 1.13. The death occurred in 21% of patients in group 1 and 4.9% of patients in group 2. The completion of TB treatment was achieved by 73.7% of patients in group 1 versus 72.7% in group 2 with $p = 0.882$ 95% CI from -0.14 to 0.12.²⁰

Only 48 patients from group 1, originally comprising 57 individuals, could be paired with patients of group 2, thus the total number of patients included in the study was 96. Other than the duration of HIV infection, there were no statistically significant differences between patients in groups 1 and 2 with respect to their social-demographic status or their clinical or laboratory characteristics at discharge from the hospital.

The average age of all patients was 34.8 years, 62.5% were males, 89.6% had attended school for 8 years

maximum and 65.6% lived in the city of Belo Horizonte. Most of the patients were single (63.5%) and in 47.9% of the cases HIV infection had resulted from sexual intercourse with men. The average duration of infection for patients of group 1 was 27.8 months (standard deviation {SD} = 39.1 months), whilst in group 2 the average was 18.1 months (SD = 33.7 months), values that were significantly different at $P < 0.001$ (Table 1). The average time of hospital confinement was 58.1 days for patients of group 1 and 48.2 days for those of group 2.

Prior to the start of the therapeutic program, 40 patients (83.3%) of group 1 presented an average T CD4+ lymphocyte count of 182.6 cells/mm³ (SD = 49.0), and 39 patients (81.3%) of group 2 exhibited an average T CD4+ lymphocyte count of 151.0 cells/mm³ (SD = 37.6). When the results were dichotomized with respect to the T CD4 lymphocyte count level of 200 cells/mm³, 68.3% of group 1 and 45.5% of group 2 have shown values below this level, a difference between groups that was not significant ($P = 0.678$). The mean value of \log_{10} (viral load) for patients in group 1 was 4.01 (equivalent to 10233 copies/mm³ of viral RNA; SD = 1.52), whilst in group 2 the mean value was 4.52 (equivalent to 33,113 copies/mm³ of viral RNA; SD = 1.34). When the results were dichotomized with respect to the median baseline HIV level for \log_{10} (viral load) of 2.6 (equivalent to 400 copies/mm³ of viral RNA), 26.5% of group 1 and 12.1% of group 2 presented values below this level, a difference between groups that was not significant ($P = 0.122$).

The average incidence of opportunistic infection prior to entry into one of the scheduled therapy programs was 3.5 for group 1 and 3.0 for group 2. Mycobacteriosis was diagnosed definitely in 34.4% of the patients, and for the majority (63.6%), the presence of *Mycobacterium tuberculosis* was confirmed. The lungs were the organs most frequently affected by the disease (47.9%). The therapy regimens employed rifampicin, isoniazid and pirazinamide (scheme S1; 57.3%), or S1 reinforced with etambutol (scheme R-S1; 25%), or one of the regimens containing streptomycin (17.7%).

Table 2 presents a comparison between groups 1 and 2 with respect to the treatment outcome for patients after one year of being discharged from hospital. In group 1, 56.3% of the patients adhered to the treatment, whilst in group 2 only 39.6% adhered to the treatment ($P = 0.102$). Moreover, 22.9% of group 1 patients abandoned the treatment during the year, whilst the percentage was much higher (54.2%) in group 2 with $P = 0.008$ and relative risk (RR) = 3.36. The number of deaths during the follow-up period was 20.8% in group 1 but only 6.3% in group 2 ($P = 0.334$). The treatment for tuberculosis was successful in 75% of the patients of group 1 and in 72.9% of group 2 ($P = 0.816$).

Table 1. Statistical comparison of the parameters, determined prior to discharge from hospital, of TB patients coinfecting with HIV who were to be supported by either an ADT (group 1) or an SAE (group 2) program

Initial parameters	P value ^a
Treatment schedule for TB prescribed for 6 months	0.669
Treatment schedule for TB prescribed for 9 months	0.668
Treatment schedule for TB prescribed for 12 months	0.374
Site of TB infection: lungs	0.414
Site of TB infection: miliary	0.665
Site of TB infection: disseminated	0.460
Site of TB infection: pleural	0.064
Site of TB infection: lymph nodal	0.653
Site of TB infection: central nervous system	0.117 ^b
Site of TB infection: osteoarticular	0.315
Site of TB infection: urinary tract	0.315
Site of TB infection: others	0.504
Source of infection: sexual intercourse with men	0.290
Source of infection: sexual intercourse with women	0.996
Source of infection: intravenous drug users	0.916
Source of infection: receivers of blood products	0.367
TB therapy employed: S1 ^c	0.149
TB therapy employed: R-S1 ^d	0.157
TB therapy employed: scheme including streptomycin	0.789
Definite diagnosis for Mycobacteriosis	0.566
Definite diagnosis for <i>Mycobacterium tuberculosis</i>	0.553 ^b
Period of HIV infection	< 0.001
T CD4+ lymphocyte count < 200 cells/mm ³	0.678
Viral load < 2.60 log ₁₀ (equivalent to 400 copies of viral RNA)	0.122

^aDetermined using the χ^2 test unless otherwise indicated.

^bDetermined using Fisher's exact test.

^cTreatment scheme S1: rifampicin, isoniazid and pirazinamide.

^dAs treatment scheme S1 but reinforced with etambutol.

Table 2. Statistical comparison of treatment outcome parameters, determined one year after discharge from hospital, of TB patients coinfecting with HIV supported by either an ADT (group 1) or an SAE (group 2) program

Treatment outcome parameters	P value ^a
Successful treatment of TB	0.816
Death after discharge from the hospital	0.334
Abandonment of treatment in the period 30 days up to 1 year after discharge from hospital	0.008 (RR: 3.36)
Adherence to treatment up to one year after discharge from hospital	0.102
Final T CD4+ lymphocyte count < 200 cells/mm ³	0.112
Final viral load < 2.60 log ₁₀ (equivalent to 400 copies of viral RNA)	0.019 (RR: 4.25)

^aDetermined using the χ^2 test; RR, relative risk.

Logistic regression analysis of the data (Table 3) indicated a significant association, within a 95% confidence interval, between abandonment of treatment and the program scheduled for group 2 ($P = 0.042$; RR = 8.09). The difference between the initial and the final mean values of the T CD4+ lymphocyte count for group 1 was 160.5 cells/mm³ (SD = 49.0) and for group 2 was 74.1 cells/mm³ (SD = 37.6). When the results from the two groups were dichotomised with respect to 200 cells/mm³, a P value of 0.112 was obtained according to the χ^2 test, indicating that the difference between the groups was not significant. The mean log₁₀(viral load) value determined one year after discharge from the hospital was reduced to 1.46 (equivalent to 29 copies of viral RNA) for group 1 patients compared with 0.73 (equivalent to five copies of viral RNA) for those in group 2, values that were not significantly different within the 95% confidence interval. However, when dichotomised with respect to the level of log₁₀(viral load) of 2.6 (equivalent to 400 copies of viral RNA) there was a significant correlation with the treatment program ($P = 0.019$) such that group 1 patients presented a 4.25-fold greater likelihood of attaining a viral load of less than 400 copies/mm³ of viral RNA compared with patients in group 2.

DISCUSSION

The only significant differences that could be detected, prior to their discharge from hospital, between patients in the two groups was that those in group 1 had been infected with HIV for a longer period than those in group 2. This is in line with the tendency to treat those patients with more complex disorders in their own homes since, if HIV-therapy is not effectively delivered, the progression of the infection results in an increase in morbidity.²¹

There was no significant difference between the success rates of the TB therapy for patients treated under the ADT or the SAE program, and treatment outcome was similar to that established in an analogous survey conducted in São Paulo in which 74% of HIV coinfecting patients attained a cure and 18% abandoned the therapy during the prescribed period.²² The TB cure rate achieved by this study were higher than the rates obtained by other national surveys with patients coinfecting with HIV who achieved TB cure rates below 58.8%.²³⁻²⁵ However, the success rates recorded for both groups of patients in the present study were lower than those observed in previous studies²⁶⁻³² of populations, containing varying percentages of HIV-infected patients, that had been treated under a directly observed therapy (DOT)

Table 3. Multivariate analysis of TB patients coinfecting with HIV who were supported by either an ADT (group 1) or an SAE (group 2) program and who had abandoned therapy during a one year period after discharge from hospital

Program	Variables ^a	P value ^b
ADT	Treatment schedule for TB prescribed for 12 months	0.847
	Source of infection: use of intravenous drugs	0.063
	TB therapy employed: S1 ^c	0.616
	TB therapy employed: scheme including streptomycin	0.877
	Definite diagnosis for Mycobacteriosis	0.143
	Site of TB infection: lungs	0.740
	Number of previous hospital confinements	0.835
SAE	Treatment schedule for TB prescribed for 12 months	0.045 (RR: 8.09)
	Source of infection: sexual intercourse with women	0.798
	Definite diagnosis for Mycobacteriosis	0.108
	Number of previous hospital confinements	0.086
	Duration of previous hospital confinements	0.220
	Gender	0.540
	Age	0.574

^aOnly variables presenting $P < 0.25$ were considered in the analysis.

^bRR, relative risk.

^cTreatment scheme S1: rifampicin, isoniazid and pirazinamide.

program. Furthermore, the number of patients who attained a cure under either treatment program in the present survey did not reach the 85% standard set by the World Health Organization.^{10,33}

Various studies have indicated that the success rate of TB therapy in patients coinfecting with HIV is low not only because of a higher rate of morbidity amongst such patients, but also because the access to such groups is more difficult.^{17,27,34} Furthermore, there is copious evidence to suggest that TB can accelerate the progression of HIV infection and thus reduce the chances of survival.^{3,35} In the present study, the rate of morbidity was higher amongst patients included in group 1 (20.8%) compared to group 2 (6.3%), although the difference was not statistically significant ($P = 0.816$). Interfering factors, such as the distribution of patients between the ADT and SAE programs, may have contributed to this result despite the similarity of the other parameters between the two groups. Since the study was of a retrospective nature, none of the parameters measured were under strict control.

Patients in the SAE program were, typically, three-times more likely to abandon their treatment than those in the ADT program. Moreover, amongst patients whose TB therapy was prolonged (i.e. ca. 12 months), those in group 2 were eight-times more likely to abandon the treatment compared with their counterparts in group 1.

Within TB treatment, the necessary levels of adherence are significantly different from those demanded for adequate HIV-treatment, mainly because of the need to control the selection pressure of HIV-resistant strains.³⁶ It is thus accepted that TB patients need to take at least 80% of the prescribed tuberculostatic drugs in order to attain a complete cure,^{19,34,36} whilst HIV-patients need to take at least 95% of the antiretrovirals prescribed for an indefinite period.^{11,12,37,38} Since the proportion of patients presenting a final load of less than 400 copies/mm³ of viral RNA was statistically superior in group 1, it is clear that adherence to the antiretroviral treatment was observed by most of the patients included in the ADT program. Therefore, it is suggested that short term TB treatments (of 6 to 9 months) for patients coinfecting with HIV can be followed-up by either ADT or SAE programs with comparable results. However, for TB treatments requiring longer periods of medication (ca. 12 months) and almost total adherence to the regime, the follow-up of HIV coinfecting patients would be more appropriate if provided under a ADT program.

The TB treatment delivered by both ADT and SAE programs offered to HIV-patients needs to be improved in order for the success rate to be raised to the levels recommended by the World Health Organization.¹⁰ New strategies must be designed in order to reach the more problematic sectors of the community including, for example, the adoption of special techniques for drug addicts and much closer collaboration with community health carers. Such work must be undertaken in an integrated manner by interdisciplinary teams

of home-carers and those from outpatient departments.³⁹ TB patients, coinfecting with HIV, for whom a long duration therapy is prescribed should preferably be assisted by an ADT program. In further considerations of ADT programs, other parameters that influence adherence to treatment must be considered, the treatment success rate and adherence must be constantly checked and compared with SAE and DOT programs,³⁷ and the follow-up period of patients must be longer than one year in order to allow for the evaluation of possible fatigue to antiretroviral adherence.⁴⁰

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