Lack of Prior Antiretroviral Therapy Is Associated with Increased Mortality Among Hospitalized Patients with AIDS in São Paulo, Brazil


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ABSTRACT

The death rate in adults with acquired immune deficiency syndrome (AIDS) at the Institute of Infectious Diseases "Emílio Ribas" in São Paulo City has decreased significantly from 29% in 1995 to 19.8% in 1999, and hospitalization time has been reduced by 4 days in the period from 1998 to 1999. Lack of antiretroviral treatment (ART) before hospitalization was associated with death during hospitalization (odds ratio [OR] 3.8), and survival was associated with previous use of three or more antiretrovirals (OR 0.15). Therefore, we recommend an aggressive campaign for human immunodeficiency virus (HIV) antibody screening among the at-risk populations in Brazil to assure that ART is provided when necessary.

INTRODUCTION

Brazil has the highest incidence of acquired immunodeficiency syndrome (AIDS) in Latin America.
More than 170,000 cases have been reported in the last 20 years, 25% of these from the city of Sao Paulo. 1 Human immunodeficiency virus (HIV) AIDS is the second cause of death of 24- to 40-year-old males in Sao Paulo. 2 A major decrease in morbidity and mortality has been reported in developed countries after the use of combined antiretroviral therapy (ART). 3 Since November 1996, the Brazilian government also has provided free public access to ART. To date, more than 50,000 HIV/AIDS patients have been treated, and a 38% decrease in the AIDS death rate from 1995 to 1997 has been demonstrated. 4,5 We have previously reported that the mortality rate in adults with AIDS after diagnosis of opportunistic infection is 2 years in Sao Paulo, 6 although local improvement in the patient care setting may also have influenced these results.

Even though HIV/AIDS is becoming a controllable disease, it is still a tremendous public health problem worldwide. Also, it has been suspected that HIV drug resistance may lead to more treatment, hospitalization, and disease progression. Therefore, in this study, we attempted to identify risk factors for AIDS death among patients who were hospitalized in November 1998 in a clinical setting where ART is widely available.

MATERIAL AND METHODS

The Institute of Infectious Diseases "Emilio Ribas" (IER) is a teaching hospital in Sao Paulo and is also the referral center for the major infectious diseases in the city. The hospital is the major reference hospital for AIDS care, with 80 beds reserved for adult patients.

Design

Clinical charts from patients with HIV/AIDS who were hospitalized during November 1998 were reviewed. This month was chosen because the weather is mild (spring), and there were no holidays or other unique factors that might affect the analysis.

Variables

Gender, risk factors for HIV transmission, time of hospitalization, estimated time for diagnosis of HIV/AIDS, and use of ART, were collected in the Microsoft Excel spread sheet. The program used in the statistical analysis was Epi Info 6.04.

Statistical analysis

All statistical tests were conducted as two-sided tests at the 5% significance level. Demographic characteristics of the survival and non-survival groups were compared using t-tests for differences between means for continuous variables (age), and a [chi]² test for categorical variables (gender, time of hospitalization, risk, and time of medication).

In addition, we have done epidemiological surveillance, such as death rate, time of hospitalization, number of deaths per 1,000 patients per year among AIDS adult patients using revised data obtained in our Statistical Section, from 1995 to 1999.

RESULTS

The mortality rate in adults with AIDS decreased significantly from 29% in 1995 to 19.8% in 1999 (p < 0.001). Also, the average hospitalization time decreased by 4 days from 20 days in 1998 to 16 days in 1999 (Table 1, data until 1997 published previously; see ref. 5). Furthermore, we noted that number of deaths for 1,000 patients per year has also been decreasing over time, from 21 in 1995 to 10 in 1999 (Table 1).
In 1998, 1,455 adult AIDS patients were hospitalized at IIER. The clinical charts of the 111 AIDS patients hospitalized in November were reviewed. Eighty-six of them were released, mean age, 35, and 25 died, mean age, 37, during that period. Sixty-four males (79%) were survivors (mean age, 35 years old) and 17 (21%, mean age, 37 years old) were nonsurvivors. Twenty-two women (73%) survived and 8 (27%) died. Mean age of survivor and nonsurvivor women was 36 and 35 years old, respectively.

The distribution of risk was as follows: 25 men who had sex with men (MSM) (23%); 22 intravenous drug users (IDU) (20%); 36 with heterosexual contacts (32%); 25 others or unknown risk (23%). There was no statistical difference between survivors and nonsurvivors regarding gender, age, risk factors, number of previous hospitalizations before outcome or type/number of previously opportunistic infections. These results are summarized in Table 2.

Table 2. Results of a Cross-Sectional Study with Data Collected from Inpatients in November 1998, at the Institute of Infectious Diseases Emilio Ribas, SP, Brazil

The length of hospitalization in November varied. The women died after 9 days and the survivor women spent 18 days in the hospital. Both survivor and non-survivor men spent a mean of 15 days in the hospital.

However, we did observe an increased risk for death among the patients with AIDS who had never had antiretroviral therapy. In 102 cases for whom we had information on ART, 31 have never taken ART previously, 19 (61%) and 12 (39%) were survivors and nonsurvivors, respectively (odds ratio [OR] = 3.85, confidence interval [C.I.] 95% = 1.29-11.71, p = 0.011, Yates corrected) compared to use of two or three more ART drugs when we analyzed the latter groups together.

We were able to determine the length of treatment in only 72 patients. In this subgroup, 9 of 56 (12%) survivors and 10 of 16 (69%) nonsurvivors had not been on ART for 10 weeks prior to admission (OR = 15.4; C.I. 95% = 3.51-73.6; p < 0.0001). Overall, the mean of time for ART was 63 and 44 weeks for the survivors and nonsurvivors, respectively. Survivors used similar time of therapy (two or three drugs), whereas patients who died, used ART less than 13 weeks for 2 and 10 weeks for 3 drugs. Double compared to triple therapy (OR = 0.39; C.I. 95% = 0.07-1.93, p = 0.31) or double compared to no taking ART (OR = 0.38; C.I. 95% = 0.11-1.29, p = 0.14), were not statistical significant when compared to triple therapy. In contrast, survival was associated with previous use of three or more antiretroviral drugs (OR = 0.15, C.I. 95% = 0.03-0.68, Yates corrected p = 0.008) when compared to naive for ART patients. All these analysis were not affected by gender, risk, or age. Time of HIV/AIDS diagnosis was estimated based on the first signal of immunessuppression, or the use of specific medication for opportunistic infection. However, most of the time the diagnosis was based on clinical observation rather than laboratory findings. The mean time of AIDS diagnosis until hospitalization in November 1998 was 118 and 66 weeks for survivors and nonsurvivors, respectively. In 97 patients, 13 of 75 survivors and 6 of 22 nonsurvivors had had AIDS diagnosis until 10 weeks previously to the hospitalization (OR = 1.6; C.I. 95% = 0.5-6.15, p = 0.4).

The most prevalent infectious disease before or during the hospitalization was tuberculosis, 30% for survivors and 44% for nonsurvivors, although toxoplasmosis encephalitis was also prevalent (20% and 28%, respectively). Curiously, among survivors, 11 (13%) had presented with suspected Pneumocystis carinii pneumonia, but only one case of Pneumocystis carinii pneumonia was recorded.
in the nonsurvivor group.

DISCUSSION

The death rate in adults with AIDS has decreased significantly from 29% in 1995 to 19.8% in 1999, and hospitalization time has been reduced by 4 days from 1998 to 1999 at our institution. The average stay in the hospital for AIDS patients in developing countries is longer than for most diseases, ranging from 15 to 80 days (Mpundu M, personal communication). In another similar study done in Rio de Janeiro, Brazil, the length of stay in a teaching hospital was 25.3 days in 1994. 7

Females died after a mean of 9 days of hospitalization, in contrast to 15 days for nonsurviving males. This finding needs further investigation, to determine if gender affects the outcome. It has been observed that women have worse clinical outcome, even with lower viral load than men 8 although these data are controversial. 9

The decreased hospitalization time noted in our study indicates that is necessary to analyze if the large-scale use of ART is cost-effective in our country, because it improves the capacity of hospital beds. Lack of ART treatment before hospitalization was associated with death during hospitalization (OR = 3.8), and survival was associated with previous use of three or more antiretrovirals (OR = 0.15). Double therapy showed similar time (76 and 64 weeks) of use when compared to triple ART among survivors, demonstrating some benefic of double therapy, even its temporary. 10

Therefore, we recommend an aggressive campaign for HIV antibody screening among the at-risk populations in Brazil to ensure that ART is provided before moderate or severe immunessuppression is established and the risk of appearance of opportunistic infections is higher, thus improving the recovery rate and avoiding the risk of death. Because patients on ART must usually visit the clinic at least once a month to obtain the medication, an added benefit is frequent follow up and improved quality of care.

ACKNOWLEDGMENT

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