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ORIGINAL ARTICLE

Clinical manifestations of treatment-naive patients with acquired immunodeficiency syndrome and responses to highly active antiretroviral therapy in the Taipei Veterans General Hospital: A 5-year prospective study

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Background: Taipei Veterans General Hospital, one of the medical centers in Taiwan, has provided highly active antiretroviral therapy (HAART) to human immunodeficiency virus/AIDS patients for more than 10 years. Five years ago, we began a prospective follow-up of our patients' clinical manifestations and responses to HAART by collecting their clinical data. In this study, we analyzed the morbidity, mortality, and responses to HAART of treatment-naive AIDS patients. The purpose was to provide local data that may be valuable in Taiwan.
Methods: Study cases were enrolled from January 1, 2004, to February 28, 2009, with inclusion criteria of newly diagnosed AIDS during hospitalization and being naive to HAART. Antiretroviral therapy was initiated. To evaluate the clinical responses to HAART, we excluded patients who were pregnant, died within 1 month after confirmation of an AIDS diagnosis, failed to initiate HAART, or were lost to follow-up for more than 6 months. Plasma viral loads and $CD4^+$ counts were quantified by reverse-transcriptase polymerase chain reaction and flow cytometry, respectively. Statistical analysis was performed using SPSS statistical software.
Results: A total of 49 patients were enrolled and 45 patients fulfilled the inclusion criteria for evaluating the efficacy of HAART. At 3 months, 12 months, and 30 months after the initiation of HAART, 64.4% (29 of 45), 88.2% (30 of 34), and 93.8% (15 of 16) had undetectable plasma viral loads, respectively, and 37.8% (17 of 45), 73.5% (25 of 34), and 81.2% (13 of

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16) had $CD4^+$ counts of more than 200 cells/μL, respectively. Median $CD4^+$ counts increased from baseline at Month 3 by 171 cells/μL and at Month 30 by 375 cells/μL. The overall mortality was 22.4% (11 of 49).
Conclusion: The virologic and immunologic responses after initiating HAART in this study demonstrated our achievements in providing care and treatment for AIDS patients during this 5-year period, which provides a strong evidence of the efficacy of HAART.

Introduction

Since 1996, the widespread use of highly active antiretroviral therapy (HAART)—a combination of at least three drugs that typically includes either a protease inhibitor (PI) or a non-nucleoside-analog reverse-transcriptase inhibitor and two nucleoside-analog reverse-transcriptase inhibitors (NRTIs)—has substantially improved the prognosis of human immunodeficiency virus (HIV)-infected patients.[1–3] There are several predictors of mortality for patients on antiretroviral therapy: viral load, $CD4^+$ count, total lymphocytes, body mass index, and adherence. Randomized clinical trials have provided strong evidence that HAART is beneficial for patients with $CD4^+$ count less than 200 cells/μL[4,5] and is also recommended for those with $CD4^+$ counts of 200—350 cells/μL.[6] However, the optimum time to start antiretroviral therapy among symptom-free patients with $CD4^+$ counts above this threshold and low or intermediate viral loads is a matter of debate.[7,8]

According to the report of the Department of Health, ROC (Taiwan), in April 2010, the seroprevalence rate of HIV infection in Taiwan was 69.8 cases per 100,000 population, with a total of 16,146 cases, which has been increasing in recent years. The proportion of males to females was nearly 11:1, and most patients were 15—39 years old, a period of known sexual activity. The proportions of newly reported HIV cases by mode of transmission in 2008 were as follows: homosexuals and bisexuals, 42%; heterosexuals, 22.6%; and intravenous drug users, 33.7%;[9] a clinical spectrum similar to those in developed countries.[10–12] All HIV-infected patients were provided with free access to inpatient or outpatient care, and antiretroviral therapy was available at 42 designated hospitals around Taiwan.

The Taipei Veterans General Hospital (VGHTPE), one of the medical centers in Taiwan, has provided care for HIV-infected patients for two decades since the first native HIV-infected patient was diagnosed at the VGHTPE in 1986. However, until now, we have not presented our achievements in mortality reduction and improving the quality of life of HIV-infected patients. In this prospective study, we have characterized the clinical spectrum, morbidity, mortality, and responses to HAART of AIDS patients in the VGHTPE during the recent 5-year period.

Materials and methods

The study cases were enrolled from January 1, 2004, to February 28, 2009. The inclusion criteria were patients newly diagnosed with AIDS during hospitalization and patients naive to HAART. Antiretroviral therapy was prescribed during hospitalization or soon after discharge on an outpatient basis. For follow-up to evaluate their clinical spectrum, morbidity, mortality, and responses to HAART, a standardized data collection form was used to record the results of all histopathological and laboratory examinations, complications associated with HIV infection, numbers and durations of hospitalizations, regimens of prophylaxis, and the antiretroviral therapy that was administered.

To evaluate the clinical responses to HAART of treatment-naive patients, cases who were pregnant, died within 1 month after confirmation of AIDS diagnosis, failed to initiate HAART, or were lost to follow-up for more than 6 months, were excluded. The HAART regimen administered and a switch of the regimen in the presence of adverse effects were according to the recommendations of the Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents, developed by the panel of the Department of Health and Human Services, USA,[6] and the Guidelines for AIDS surveillance and treatment published by the Center for Disease Control in Taiwan. Plasma viral loads (PVLs) and $CD4^+$ counts were checked before HAART and at 1 month and 3 months after initiating ART. If the virologic, immunologic, and clinical responses were satisfactory, PVLs and $CD4^+$ counts were followed up every 6 months thereafter. Outcome measures were the proportions of patients with undetectable PVLs (<50 copies/mL) and changes of $CD4^+$ counts, calculated according to the data checked at Months 3, 6, 12, 18, 24, 30, 36, 42, 48, 54, and 60, after initiating HAART.

PVLs were quantified using reverse-transcription polymerase chain reaction with a Roche COBAS TaqMan 48 real-time PCR analyzer (F. Hoffman-La Roche, Basel, Switzerland). $CD4^+$ counts were evaluated by flow cytometry (FACS Calibur; Becton-Dickinson Diagnostic Instrument System, Sparks, MD, USA). Hemograms and blood biochemistries were also determined with the same blood sampling scheduled for quantifying PVL and the $CD4^+$ count.

Categorical variables were compared using a Pearson Chi-square test in terms of the virologic efficacy of HAART between patients with baseline PVL of higher and lower than 5 $\log_{10}$ copies/mL and baseline $CD4^+$ counts of higher and lower than 50 cells/μL. Cox proportional-hazards regression was used to estimate the influence of the baseline PVL and $CD4^+$ count on the immunologic response of the $CD4^+$ count after initiating HAART. We used Kaplan—Meier survival analysis to estimate any correlation between patients' mortality with baseline PVL and $CD4^+$ counts. Statistical analysis used SPSS statistical software (Version 17.0; SPSS Inc. Chicago, IL, USA). A p value less than 0.05 was considered to be statistically significant.