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Research Article

Immunological and clinical progress of HIV-infected patients on highly active antiretroviral therapy in north west Ethiopia

Kuzey Batı Etiyopya'da yüksek etkili antiretroviral tedavi alan HIV-enfekte hastaların immünolojik ve klinik gelişimi

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Abstract
The survival benefits of highly active antiretroviral therapy (HAART) in HIV infected patients have been studied well in the developed world. In resource poor settings like Ethiopia such treatment was started only in 2003. As a result, the existing treatment guidelines and recommendations are based on data from the developed world. The objective of this study was to determine the immunological and clinical progress in HIV/AIDS patients in one year data review of patients' card who initiated on HAART in Ethiopia. A retrospective cohort study was done based on past medical records of HIV/AIDS patients, using a structured data collection format. All patient cards of one year data with patients who initiated HAART from October 1, 2006 to November 30, 2007 were included in the study. The data collected was analyzed using SPSS for window version 16.0. The majority of the study population (383, 64.2%) were prescribed zidovudine/lamivudine/neverapine (ZDV/3TC/NVP) regimen initially. Overall functional status change showed that ability to work was increased by 31.5%, being ambulatory decreased by 93.4% and bedridden status decreased by 80%. A total of 240 (46.9%) patients have showed functional status improvement. Average mean weight change of 5.9 kg (increment by 11.9%) was seen during a one year follow-up. The patients showed immunological change from 132.883 mean CD4/mm^3 count to 335.87 mean CD4/mm^3. About 492 (82.4%) patients present with different type of opportunistic infections (OIs) at start of therapy which dramatically dropped to only 40 (6.7%) patient after one year of receiving HAART. HAART initiation has decreased progression of the diseases and improved the patients' quality of life. Most patients have showed a significant increment in their CD4 count. The restoration of CD4 in turn has improved the clinical status of most patients. Despite the significant progression of health of patients, greater immunological and clinical success should be attained by encouraging patients for effective use of those lifesaving drugs with maximal adherence.
Keywords: CD4 count; clinical progress; HAART; immunological progress

Özet
HIV ile enfekte hastalarda yüksek etkili antiretroviral tedavinin (HAART, *highly active antiretroviral therapy*) yaşam üzerindeki faydaları gelişmiş ülkelerde çok çalışılmıştır. Etiyopya gibi kaynakları kısıtlı yerlerde bu gibi tedavi 2003'de başladı. Sonuç olarak, var olan tedavi kılavuzları ve tavsiyeler gelişmiş ülkedeki verilere dayanmaktadır. Bu çalışmanın amacı, Etiyopya'da HAART tedavisine başlanan hasta kartlarındaki bir yıllık veri incelenerek HIV/AIDS hastalarının immünolojik ve klinik gelişimi saptamaktı. Retrospektif kohort çalışma, yapılandırılmış veri toplama formatı kullanılarak HIV/AIDS hastalarının geçmişteki tıbbi kayıtlarına dayanarak yapıldı. 1 Ekim 2006'dan 30 Kasım 2007'ye kadar HAART tedavisi başlanan hastaların kartlarındaki bir yıllık veriler çalışmaya alındı. Toplanan veriler SPSS for Windows sürüm 16.0 kullanılarak analiz edildi. Çalışılan popülasyonun büyük çoğunluğu (383, %64.2) başlangıçta zidovudin/lamivudin/neverapin (ZDV/3TC/NVP) tedavisi verilmişti. Genelde fonksiyonel durum değişimi, çalışma yeteneğinin %31.5 arttığını, ayakta tedavi edilmenin %93.4 azaldığını, yatağa bağlı kalma durumunun %80 azaldığını gösterdi. Toplam 240 hasta fonksiyonel durum düzelmesi gösterdi. Bir yıllık izleme sırasında 5.9 kg ortalama ağırlık değişimi (%11.9 artma) gözlendi. Hastalar ortalama 132.883 CD4/mm^3 sayımından ortalama 335.87 CD4/mm^3'e immünolojik değişim gösterdi. Tedavinin başlamasında farklı tipte fırsatçı enfeksiyonu bulunan yaklaşık 492 (%82.4) hasta, HAART tedavisi başlamasından bir yıl sonra dramatik olarak sadece 40'a (%6.7) düştü. HAART tedavisi başlanması hastalığın ilerlemesini azalttı ve hastaların yaşam kalitesini iyileştirdi. Hastaların çoğu CD4 sayılarında anlamlı artışlar gösterdi. CD4'deki düzelme birçok hastanın klinik durumunu iyileştirdi. Hastaların sağlığındaki anlamlı iyileşmeye karşın, hayat kurtaran bu ilaçlara daha fazla etkin kullanılması için hastaların teşvik edilmesi ile daha fazla immünolojik ve klinik başarı elde edilmelidir.
Anahtar kelimeler: CD4 sayımı; klinik gelişim; HAART; immünolojik gelişim

Introduction

Human immunodeficiency virus (HIV) epidemic in Ethiopia started in the early 1980's. Based on recent sentinel surveillance data, the national adult prevalence rate is estimated at 6.6% (1). The introduction of highly active antiretroviral therapy (HAART) in 1997 has markedly improved the length of survival and the morbidity of HIV-infected patients through the improvement of the immunodeficiency caused by HIV infection (2-10). In recent years, the management of human immunodeficiency virus positive individuals has been based on HAART comprising a combination of nucleoside analogue reverse transcriptase inhibitors and at least one protease inhibitor and/or one non-nucleoside analogue reverse transcriptase inhibitor (11).

The risk to develop AIDS clearly depends on immune reconstitution and viral suppression during therapy, and prognosis is best for patients who show both recovery of CD4 cell counts and sustained viral suppression (12,13). In clinical trials, HAART has been shown to suppress viral load (VL) to less than the limits of detection and to increase the CD4+ T lymphocyte percentage in many

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patients (14,15), with good outcomes overall (16,17). Results from observational studies suggest that at least 73.5% of patients initiating HAART achieve complete virological suppression within 6 months (18), but 9%–45% of patients do not experience an appropriate increase in their CD4 cell counts in the short term (19, 20). While an increase in total CD4+ T lymphocytes is readily detectable, the ability to regenerate immunocompetent T-cell populations remains unresolved (21). Some clinical trials have demonstrated that the regenerated T cells consist predominantly of the memory (CD45RO+) type (14), while others have shown repopulation of naive (thymus-dependent, CD45RA+) T cells as well (22).

The survival benefits of HAART in HIV infection have been studied well in the developed world. In resource poor settings, such treatment was started only recently. As a result, the existing treatment guidelines and recommendations are based on data from the developed world (23). Only few data concerning the immunological and CD4+ cell count change and clinical outcomes like occurrence of opportunistic infections and improvement in the quality of life, in developing countries have been published since the advent of HAART. Therefore, the aim of this study was to assess the immunological and clinical progress in HIV/AIDS patients who started HAART by (1) describing the change in the median weight of the patients after 6 and 12 months of HAART, (2) determining the functional status change after 6 and 12 months of HAART, (3) describing the median CD4 cell count change after 6 and 12 months of HAART, (4) assessing the relation between CD4 cell count at the start and mortality during the 12 months of HAART, (5) determining the prevalence of side effects during the 12 months of HAART and (6) determining the change in the occurrence of opportunistic infections during the twelve months of HAART follow-up.

Participants and methods

Study setting

Assessment of immunological and clinical progress of HIV/AIDS patients receiving HAART service was conducted from January 10 to February 30, 2010 in Felegehiwot Referral Hospital in Northwest Ethiopia. The hospital is the governmental hospital found in Bahir Dar City in Amhara Regional State and provides many types of health services to the public including the HAART services.

Study design

A retrospective cross-sectional study based on the past medical records of HIV/AIDS patients on HAART services in the hospital was conducted. The data was a data on the patients' medical records that are filled by physicians during the one year of HAART follow up in the hospital. All HIV/AIDS patients living who were receiving HAART services in Felegehiwot Referral Hospital since the start of HAART program. All HIV/AIDS patients who initiated HAART from October 1, 2006 to November 30, 2007 in the Hospital were included in the study. The exclusion criteria includes; patient cards which are incomplete for the study, patient cards of HIV/AIDS patients less than 18 years of age, patient cards of pregnant females during the one year, patient cards of transferred-out patients and patient cards of transferred-in patients from other HAART clinics.

Data collection

A structured questionnaire was prepared to collect the information. The validity of the questionnaires was assessed through in-depth discussion with experienced professors and internist working in College of Public Health and Medical Science of Jimma University. The questioners included patient information, HAART regimen at start, initial clinical stage of patients, CD 4 Cell count, Follow up status, change in median weight, HAART side effects occurred, functional status, medication adherence, change in median CD4cell count, and change in the status on opportunistic infections. Before the actual data collection process the prepared data collection format was pre-tested on 25 patient cards and necessary corrections was made accordingly.

Data analysis

The collected data was cleared, categorized, and coded. All data collected were then analyzed using the Statistical Package for the Social Sciences (SPSS) software program (version 16.0, Chicago, IL, USA). The immunological and clinical progress was reported as percentage.

Ethics

This study was approved by the Ethics Committee of Jimma University. Then official letter was written to the hospital to obtain their permission to undertake the research. The collected data from the patients' medical records was kept confidential and code number rather than name was used in the data collection process.

Results

Sociodemgraphic characteristics

A total of 597 HIV/AIDS patients' cards were included in this study. From these, the majority, 367 (61.5%), were females. The mean age of the participants was 28.4±9.5 years (mean±SD). Over 90% of the patients were Orthodox Christian by religion. The education status of the study population showed that 219 (36.7%) were secondary, 198 (33.2%) were illiterate, 123 (20.6%) primary and 57 (9.5%) tertiary. Out of total study populations 311 (52.1%) were married, 130 (21.8%) were divorced and 76 (12.7%) were widowed.

HAART regimen at start

The majority of the study population, 383 (64.2%), were prescribed zidovudine/lamivudine/neverapine (ZDV/3TC/NVP) regimen, followed by 158 (26.5%), 27 (45%), 26 (4.4%), 3 (0.5%) patients with stavudine/lamivudine/neverapine (D4 T30/3TC/NVP), stavudine/lamivudine/efevirenz (D4T 30/ 3TC/EFV), zidovudine/lamivudine/efavirenz (ZDV /3TC/ EFV) and stavudine/lamivudine/neverapine (D4T 40/3TC/NVP) respectively (Table 1).

Table 1. HAART regimen at start.

Regimen	*Sex*		*Total* (%)
	Male (%)	Female (%)	
D4 T30/3TC/NVP	41 (25.9)	117 (74.1)	158 (26.5)
D4T 40/3TC/NVP	2 (66.7)	1 (33.3)	3 (0.5)
D4T 30/ 3TC/EFV	12 (44.4)	15 (55.4)	27 (4.5)
ZDV/3TC/NVP	160 (41.8)	223 (58.2)	383 (64.2)
ZDV /3TC/ EFV	15 (57.7)	11 (42.3)	36 (4.4)
Total	230 (38.5)	367 (61.5)	597 (100)

Medication adherence to HAART and prevalence of side effects

Among all study population 196 (32.8%) male patients had good adherence, 30 (5%) fair, 4 (0.7%) poor and from females 287 (48.1%) had good, 71 (11.9%) fair and 9 (1.5%) poor adherence. Totally 483 (80.9%) patients had good, 101 (16.9%) fair and 13 (2.2%) are poor. Seventy eight (13.1%) patients experienced clinically significant side effects of HAART. Zidovudine related anemia was observed in 43 (7.2%) patients, neverapine related allergic dermatitis was seen in 14 (2.3%) patients, nausea and vomiting in 13 (2.2%) patients, stavudine related peripheral neuropathy in 5 (0.84%) patients and efavirenz related central nervous toxicity was seen 3 (0.5%) patients.

Functional status change

At HAART start 445 (74.5%) were working, 137 (23%) were ambulatory and 15 (2.5%) were bedridden patients. After 12 month follow up 585 (98) patient were able to work, only 9 (1.5%) patients became ambulatory and 3 (0.5%) patients became bedridden. Over all functional status change showed that ability to work increased by 31.5%, being ambulatory decreased by 93.4% and bedridden status decreased by 80%. A total of 240 (46.9%) patients have showed functional status improvement (Table 2).

Table 2. Change in functional status after a year of receiving HAART.

Functional status	*Change in functional status*		*Difference* (%)
	At start of treatment (%)	After 1 year of treatment (%)	
Working	445 (74.5)	585 (98.0)	140 (31.5)
Ambulatory	137 (23.0)	9 (1.5)	128 (93.4)
Bedridden	15 (2.5)	3 (0.5)	12 (80.0)

Change in mean weight

From total study population males have 54.4 kg mean weight at HAART start and 60.4 kg after 12 months of follow up. The means weight change for males is 6 kg (SD=±5.4). Females have 47.1 kg means weight at HAART start and 53.1 kg after 12 month with a mean weight change of 5.9 kg (SD=±6.3). Total study population mean weight at HAART start was 49.9 kg while after 12 months it was 55.9 kg with over all mean weight change 5.9 kg (SD=±5.8)which increased by 11.9% (Table 3).

Table 3. Clinical and immunological response after the twelve months of HAART follow up.

Clinical parameter	*Sex*		*Total Mean*
	Male	Female	
Mean weight of the patients			
At start of treatment	54.4	47.1	49.9
After 1 year of treatment	60.4	53.05	55.9
Change in mean weight	6.0 (11.0%)	5.9 (12.6%)	5.9 (11.9%)
Mean CD4 Cell Count			
At start of treatment	119.2	141.5	132.9
After 1 year of treatment	313.9	349.6	335.9
Change Mean CD4 Cell Count	194.8 (163.5%)	208.2 (147.1%)	203.0 (152.8%)
Occurrence of opportunistic infections			
At start of treatment	301	191	492
After 1 year of treatment	29	11	40
Change occurrence of opportunistic infections	272 (90.4%)	180 (94.2%)	452 (91.9%)

Mean CD4 cell count change

From total study population males have 119.16 mean CD4/mm^3 at HAART start while after 12 months it became 313.93 CD4/mm^3 with a change of 194.77 mean CD4/mm^3 (SD=±21.5) or 163.45% increment. Females have 141.48 mean CD4/mm^3 at HAART start and 349.63 mean CD4/mm^3 after 12 months of follow up showing 208.15 mean CD4 change (SD=±25.7) or 147.1% immunological improvement. Totally the whole sample population showed immunological change from 132.883 mean CD4/mm^3 count to 335.87 mean CD4/mm^3 (Table 3).

Change in the occurrence of opportunistic infection

From total study population, 492 (82.4%) present with different type of opportunistic infections at HAART start which dramatically dropped to only 40 (6.7%) patient after one year of receiving HAART. In males opportunistic infections decreased by 90.4% and in females decreased by 94.2% (Table 3).

Discussion

The therapeutic objective of HAART is to suppress viral replication and to induce the highest possible degree of immune restoration, with the ultimate goal being to delay or prevent the progression of clinical disease. Various randomized clinical trials (24-29), have shown that 60%–90% of patients treated with HAART achieved sustained suppression of viral load below the detection limit of standard assays.

As it has been reported in other studies (25,30-34) HAART produced a substantial increase in CD4 cell counts in our study. In this study, with initial over all baseline mean CD4 count of 132.9 cells/mm^3, showed a mean increase in CD4 count of 203.0 cells/mm^3. Touloumi et al. (24) showed that increase in CD4 cell counts is biphasic. It is believed that the initial rapid increase in CD4 cell counts is a result of the redistribution of trapped memory T cells into the

peripheral blood from the lymph nodes together with a decrease in activation-induced apoptosis. This initial phase is followed by a slower repopulation of newly produced naïve T cells. The repopulation is slow and gradual.

The restoration of CD4 count by HAART normally increases the clinical status of patients like weight, functional status and decrease occurrence of opportunistic infections. However, in a community based HAART program in Cape Town, South Africa although 78.6% of patients receiving HAART have fully suppressed viral load at 2 years. It was found out that the death rate in the first three months after enrollment was 6% (35).

There are various conflicting findings in literature about the course of immunological, virological and clinical parameters according to sex. Some studies have found higher CD4 cell counts in women (36,37); other found higher CD4 cell counts in men (38), and still others found similar values in both sexes (39,40). It has also been reported that there are greater declines in CD4 cell counts in women (41) or no differences with men (42), as well as greater increases in CD4 cell counts following HAART in women (43) or no differences with men (44). We found higher CD4 cell counts at baseline (141.48 mean CD4/mm^3 vs. 119.16 mean CD4/mm^3) and after one year (showing 208.15 mean CD4 increment vs. 194.77 mean CD4/mm^3) in female which is in agreement with the higher CD4 cell counts observed in previous studies (36,37,45).

In this study both sexes showed comparable increment in mean body weight. Males have shown 6 kg increscent from mean baseline weight of 54.4 kg, while females have showed a 5.9 kg increment from mean base line weight of 47.1 kg. In one study, the result showed that an overall sample population showed a mean weight change of 5.8 kg (46) similar to current study. Collazos et al. (47) however, showed that women have more favorable clinical and viroimmunological patterns than men both at baseline and during antiretroviral treatment. Sex has a small but significant influence on the clinical and laboratory outcomes of HIV infection.

The other parameter that indicates the clinical progress of HIV/AIDs patients is functional status change. In this study, from a total of 152 ambulatory or bedridden patients at HAART start, 140 (92%) patients showed functional status improvement (either from ambulatory to working, bedridden to ambulatory or bedridden to working). The other parameter used to determine the clinical progress is occurrence of opportunistic infection. Initially, 82.4% patients have some type of opportunistic infections. The reduction of occurrence of opportunistic infections was decreased by 91.9% from 492 to 40 patients. However, other study showed that only 62% of patients have opportunistic infections at HAART start and after 12 months follow up almost all patients became free of opportunistic infections (17). The figure difference may be due to difference in the quality and type of medications used in the two countries and the living standard or quality life difference of the people which may affect the occurrence of opportunistic infections.

Current trends are designed to maximize the number of patients who can gain access to HAART treatments and adhere to medications. In this study, over 80% of the patients showed good adherence. HAART often comprises complex regimens, high pill burdens and the potential for various adverse effects and toxicities from the medications. In this study the majority of the patients (7.2%) showed zidovudine related anemia. We did not find differences between sexes regarding side effects of medications. But, several previous study found a trend towards a higher rate of adverse effects in women compared with men, which have been explained in terms of higher exposure to these drugs in women (44) or different expression and activities of drug transporters and metabolizing enzymes (48). In fact, women seem to reach higher plasma concentrations with a number of antiretroviral drugs compared with men (49).

In conclusion, the finding of the study suggests that HAART initiation has decreased progression of the diseases and improvement in patients' quality of life. Most patients have showed a significant increment in their CD4 count. The restoration of CD4 in turn has improved the clinical status of most patients. They have showed considerably big change in their weight and functional status of patients. In addition, occurrence of opportunistic infection has reduced dramatically. Despite the significant progression of health of patients, greater immunological and clinical success should be attained by encouraging patients for effective use of those life saving drugs with maximal adherence.

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