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Research Article

COMPARATIVE STUDY OF THE EFFECTS OF ANTIRETROVIRAL THERAPY (ART) ON CD_4 CELL COUNT IN JIMMA UNIVERSITY SPECIALIZED HOSPITAL, JIMMA TOWN, OROMIA REGION, ETHIOPIA

Alemayehu Lelisa Duga[1]*, Gizat Molla Kassie[2], Boressa Adugna Horsa[3]

[1]Responsible Pharmacist, Health quest Pharmaceutical Company, Manzini, Swaziland

[2]Clinical Pharmacist and Lecturer, Department of Pharmacy, College of Public Health and Medical Sciences, Jimma University Jimma, Ethiopia

[3]Pharmacist and Lecturer, School of Pharmacy, College of Medicine and Health science, University of Gonder, Ethiopia

*Corresponding Author Email: firaollelisa@gmail.com

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ABSTRACT

The treatment option for AIDS have drastically changed since 1987 when the first drug of HIV/AIDS Zidovudin (ZDV) was approved, mono therapy has been replaced by the most effective currently is HAART which includes three drugs from one or all the three categories to decrease incidence of viral resistance. From about, 1,387,039 people living with HIV/AIDS in Ethiopia 167,271 people were initiated on ART by October 2009. The aim of this study is to determine comparative effects of ART on $CD4^+$ cell count in Jimma University Specialized Hospital and assess comparative effects of ZDV and d4T based combinations on $CD4^+$ cell count, to assess comparative effects of EFV and NVP based combinations on $CD4^+$ cell count. Cross-sectional retrospective study was employed. Data (from June 2006 to October 1, 2013) was collected from patient records using data collection format to determine comparative effects of ART regimen on $CD4^+$ cell count in Jimma university specialized hospital. One hundred twenty three patients fulfilled the inclusion criteria and were studied. At six month the EFV based regimens CD_4^+ cell count had increased with mean of 332 cells/mm^3 in the ZDV/3TC/EFV (n = 4) (baseline 139 cells/mm^3), a mean of 302.36 cells/mm^3 in the d4T/3TC/EFV (n = 11) (baseline 102.82 cells/mm^3) and a mean 283.06 cells/mm^3 in the TDF/3TC/EFV (n = 17) (baseline 110.06 cells/mm^3). The mean CD_4^+cell count recoveries of EFV and NRTIs were higher than NVP and NRTIs. ZDV/3TC/EFV mean CD_4 count was greater than TDF/3TC/EFV.

Keywords: HIV/AIDS, CD_4^+cell count, HAART, Viral resistance, ART Regimen

INTRODUCTION

The treatment option for AIDS have drastically changed since 1987 when the first drug for HIV/AIDS Zidovudin (ZDV) was approved by the Food and Drug administration (FDA), even though there is still no cure for it. Mono therapy has been replaced by highly active antiretroviral therapy (HAART), which has reduced the incidence of viral resistance. As a high viral load is associated with HIV related morbidity and mortality, the goal of Antiretroviral therapy (ART) is to achieve Human immunodeficiency virus (HIV) viral suppression and reduce the level of HIV RNA to as low as level as possible, for as long as possible, restore and preserve immunological function, improve quality of life, reduce HIV related morbidity and mortality and reduce HIV transmission from mother to new born children[1,2]. In 2003 the government of Ethiopia introduced its ART program and the country launched free ART in 2005[5]. In October 2009 about 167,271 people living with HIV/AIDS (PLWHA) were initiated on ART and 497 hospitals and health centers are providing HIV care and treatment service in all regions of the country[3]. Currently there are three main categories of ARV drugs such as Nucleotide Reverse Transcriptase Inhibitors (NRTI), Non-Nucleotide Reverse Transcriptase Inhibitors (NNRTI) and Protase Inhibitors (PI) available for clinical use, although the number and category of drugs are increasing from time to time. These drugs are given in different regimens; the most effective currently is HAART which includes at least three drugs from one or all the three categories[4]. The current recommended preferable first line regimens for treatments of adults and adolescents naïve patients in Ethiopia consists of NRTIs backbone with one of the NNRTIs. Stavudin/Lamivudin/Neverapine (ZDV/3TC/NVP) or Efaverence (EFV) and Stavudine (d4T)/3TC/NVP) or EFV and in selective setting when the standard first line regimens may not possible Tenofovir (TDF)/3TC/NVP or EFV and Abacavir (ABC)/3TC/NVP or EFV regimens are given as first line. In the event of first line treatment failure, there is indication to start second line regimens didanosine (ddI) or TDF/ABC/LPV/ritonavir(r) or Sanquinavir (SQV)/r or Nelfenavir (NFV) or Indinavir (IND)/r or Atazanavir (ATV)/r[5]. According to recent WHO guideline recommended first line ARV regimens in adults and adolescents naïve patients consists: AZT/3TC/NVP or EFV and TDF/3TC or FTC/NVP or EFV, where as d4T or AZT/3TC/ATV/r or LPV/r, TDF/3TC or FTC/ATV/r or LPV/r and rarely ddI and ABC included regimens are second line treatments[6]. Effective ART should restore and preserve immunological function. The effectiveness of ART is assessed by clinical observation, determination of CD_4 cell count and plasma viral load. As viral load determination is not normally available in resource limited setting it is recommended that programs primarily use clinical observation and where possible CD_4 count criteria[7]. The multicenter international study enrolled 1,216 treatment naïve patients from 67 sites in 17 countries on five continents including from Europe, South Africa, Australia, Thailand, South America and USA to determine comparative effects of Stavudin/Lamivudin/Neverapine (d4T/3TC/NVP) Vs Stavudin/Lamivudin/Efaverenze (d4T/3TC/EFV) on baseline median CD_4^+ cell count just below 200 cells/mm^3 (range 70-330), age 40. CD_4^+ increases for patients completing the study increased similarly and were 170 cells/mm^3 and 190 cells/mm^3 at 48 weeks in NVP and EFV based regimens respectively, with no statistically significant difference between regimens[8]. A prospective cohort study conducted in Cameroon on total of 169 patients was enrolled between

January 2001 and April 2003; 85 of them received ZDV/3TC/NVP and 84 received d4T/3TC/NVP. Most of the patient characteristics were similar in the ZDV and d4T groups. However, compared to patients in the d4T group, those in the ZDV group had known their HIV sero status for a longer time (37.5 VS 20.2 months) and they also had a higher viral load (5 log 10 copies/ml, 67 % VS, 57 %). In contrast, the CD_4 cell count tended to be higher in ZDV group patients than in those receiving a d4T based regimen (152 Vs 117/mm^3), although the difference did not reach statistical significance[9]. A retrospective study conducted in Australia to assess and compare the efficacy and safety of three triple combination antiretroviral therapies in seventy HIV-1 infected treatment naïve adult patients with CD_4^+ T-cell counts >50 cells/mm^3 were randomized to receive either ZDV/3TC/NVP, d4T/ Didanosine(ddI)/NVP or d4T/3TC/NVP for 52 weeks. The mean increases in CD_4^+T-cell counts in the AZT/3TC/NVP, d4T/3TC/NVP and d4T/ddI/NVP group were 139,113 and 174 cells/mm^3 respectively[10]. A prospective randomized study conducted at 81 centers in United States, South America and Europe from June 9,2000 to January 30, 2004 on a total of 753 patients infected with HIV who were ART naïve were screened and 602 patients entered the study; 299 of them received (TDF)/3TC/EFV and 303 received d4T/3TC/EFV. The baseline mean CD_4^+ T cell counts were 276 cells/mm^3 in TDF/3TC/EFV group and 283 cells/mm^3 in d4T/3TC/EFV group. At the end of three years study, the mean CD_4^+ T-cell count of TDF/3TC/EFV and d4T/3TC/EFV increased by +263 cells/mm^3 and +283 cells/mm^3 respectively[11]. In a retrospective cohort study conducted in Thailand in all ART naïve patients who were receiving rifampicin between January 2002 and December 2005; of 188 patients, 77 and 111 patients were initiated on EFV based ART and NVP based ART respectively. Over all, median (inter quartile range (IQR) CD_4^+ count was 36(15-77) cells/mm^3. At 24 and 48 weeks, respective median CD_4^+ counts were 174 and 254 cells/mm^3 in the EFV group and 156 and 218 cells/mm^3 in the NVP group[12].

MATERIALS AND METHODS

The study was conducted in JUSH located in Jimma town, Oromia regional state about 348 km south west of the capital Addis Ababa. JUSH is one of the biggest health services delivering hospital in Oromia region. There were about 2707 PLWHA on ART follow up. JUSH was chosen for this studies mainly because of fact that, it is one of the main specialized and teaching hospitals of the country with separate clinic for PLWHA and portable to collect data. Thus good combination of sample groups even from the nearby rural areas with different living styles could be included in the study. A Cross-sectional retrospective study on data (from June 2006 to October 1, 2013 G.C) collected from patients records using data collection format was designed to assess the comparative effects of ART combination on CD_4^+ count in JUSH from January 18 to 29, 2014 G. C. All PLWHA who were on HAART in JUSH were the source population for the study population was source of the study. All PLWHA individuals age greater than 15, non-pregnant and who treated with the same regimen at least for six month. Each participant must have had CD_4^+ cell count records of baseline and at six month. Data was collected only from patient cards accessible during data collection. Potential participants were excluded if there were insufficient data to be included in the analysis.

Ethical Consideration

The data collection was started after getting full consent from administrative bodies of Jimma University Specialized Hospital (JUSH). The student research programme office of Jimma University offered a letter for the administrative bodies of the hospital.

RESULTS

A total of 2595 PLWHA were initiated on HAART from June 2006 to October 1, 2013 at JUSH. But during data collection only 1553 patients' cards were available in data room. Among these, 27 were dead, 61 were dropped, 7 were lost to follow up, 64 were switched treatment regimen, 51 were transferred out to other health fertilities and 80 were under fifteen children. A total of 1021 PLWHA on HAART had incomplete CD_4 cell count records of either baseline or at 6^{th} month. Only 123 PLWHA fulfilled the inclusion criteria and were included in study. Most patients (62 %) were on d4T/3TC/NVP and 3 % of the patients were on ZDV/3TC/EFV regimen (Figure 1).

The mean age at initiation of therapy was 31.89 (SD = 8.29) and the majority (62.6 %) of the participants were females. Mean baseline CD_4^+ count of the study population was 146.84 cells/mm^3 (SD = 99.61) with females patients having higher CD_4^+ count than male patients (Table 1 and Table 2).

A mean CD_4^+ count of d4T/3TC back bone EFV based regimen increase from baseline 102.82 cells/mm^3 (SD = 51.31) to 302.36 cells/mm^3 (SD = 160.62) was significantly higher than the same backbone NVP based regimen increase from baseline 165.18 cells/mm^3 (SD = 109.98) to 282.63 cells/mm^3 (SD = 142.61) was observed at 6^{th} month after initiation of HAART. In similar manner, the ZDV/3TC backbone combination of EFV [mean baseline $CD4^+$ count 139 cells/mm^3 (SD = 66.81)] increase to 332 cells/mm^3 (SD = 111.94) have higher immunological success than the same backbone NVP based regimen (mean baseline CD_4^+ count 129.93 cells/mm^3 (SD = 74.72) increase to 257.27 cells/mm^3 (SD = 155.13). The TDF/3TC/EFV mean CD_4^+ cell count increase from baseline 110.06 cells/mm^3 (SD = 83.306) to 283.06 cells/mm^3 (SD = 142.03) at 6^{th} month was lower than other EFV based regimens, but higher than NVP based regimens (Figure 2, Table 2 and Figure 3).

Females showed better mean CD_4^+ cell count change outcome than males in d4T/3TC/EFV, ZDV/3TC/NVP and ZDV/3TC/EFV while males showed better mean CD_4 cell count change than females in d4T/3TC/NVP and TDF/3TC/EFV at the end of 6^{th} month treatment (Figure 4)

DISCUSSION

The comparative study of ART regimens on the HIV infected patients enrolled for ART treatment at JUSH showed different success in immunological recovery at the end of sixth month after initiation of treatment. Compared to the mean CD_4^+ cell count increase of d4T/3TC/NVP combination from baseline mean CD_4^+ count 165.18 cells/mm^3 (SD = 109.98) to 282.63 cells/mm^3 (SD = 142.61), the mean CD_4 cell count increase of d4T/3TC/EFV from baseline mean 102.82 cells/mm^3 (SD = 51.31) to 302.36 cells/mm^3 (SD = 160.62) have shown higher CD_4 cell count achievement.

Table 1: Socio–demographics of PLWHA at enrolment in JUSH, from June 2006 to October 1, 2013

Characteristics	Frequency	Percentage
Female	77	62.6
Male	46	37.4
Total	123	100

Table 2: Clinical characteristics of PLWHA at enrollment in JUSH, from June 2006 to October 2013

Clinical characteristics	Treatment regimen	Female	Male	Total (Average)
Mean CD_4^+ cell count (cells/mm^3)(SD)	d4T/3TC/NVP	170.02	157.77	165.18 (109.98)
	d4T/3TC/EFV	125.67	75.4	102.82 (51.31)
	ZDV/3TC/NVP	145	107.33	129.93 (74.72)
	ZDV/3TC/EFV	112	166	139 (66.81)
	TDF/3TC/EFV	98.64	163.33	110.06 (83.306)
Total (average)	-	149.16 (110.61)	142.96 (78.82)	146.84 (99.61)
Mean age [yr (SD)]	-	30.06 (8.02)	34.96 (7.89)	31.89 (8.29)

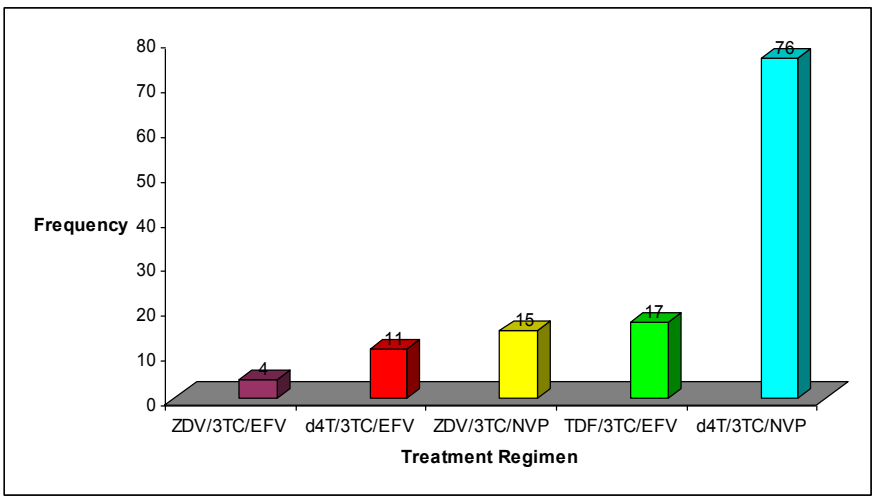

Figure 1: Types of treatment regimens of PLWHA used in JUSH, from June 2006 to October 1, 2013

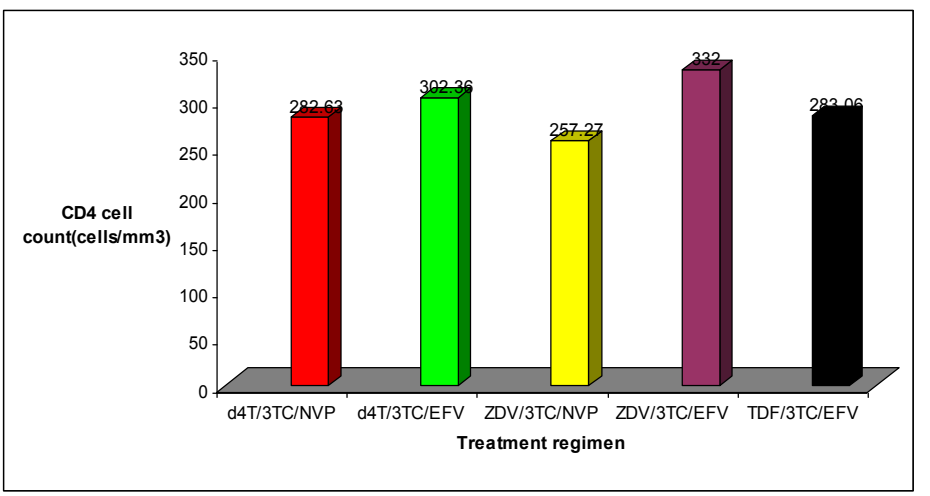

Figure 2: Comparative effects of treatment regimens on mean CD_4^+ cell count in PLWHA in JUSH, from June 2006 to October 1, 2013

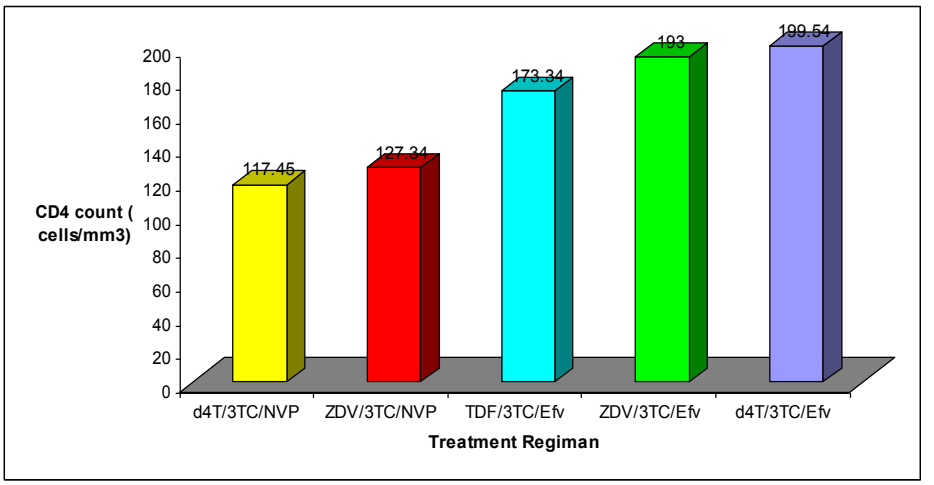

Figure 3: The comparative mean CD_4 count net increase of treatment regimens in PLWHA in JUSH, from June 2006 to October 1, 2013

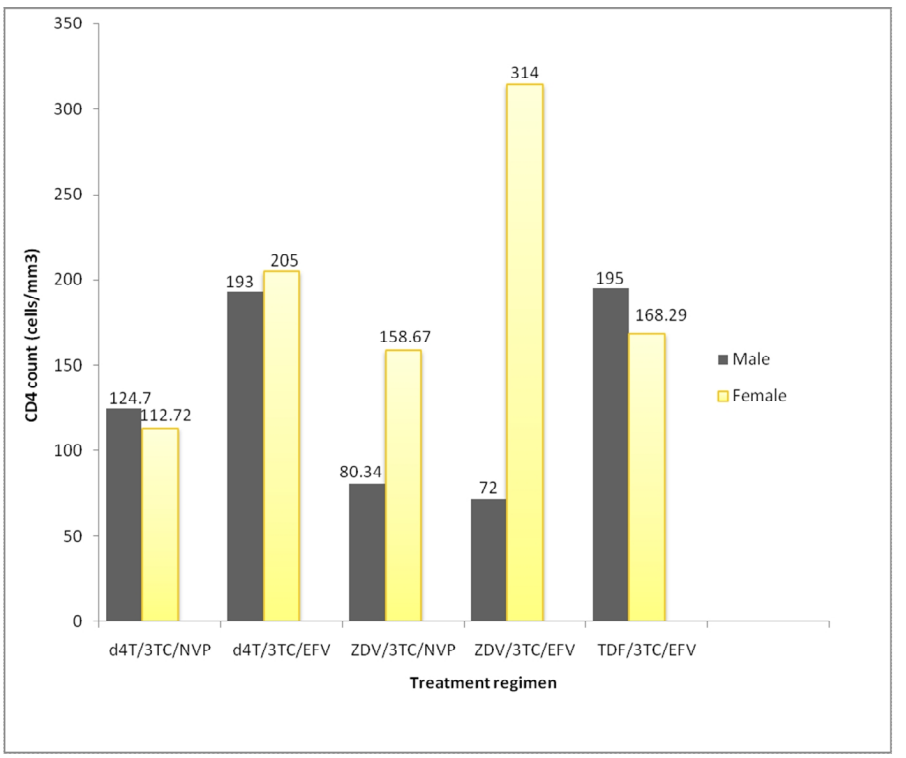

Figure 4: Comparative net increase mean CD_4^+ cell count of treatment regimens on different sex in PLWHA in JUSH, from June 2006 to October1, 2013

These findings are comparable with the multicenter international study conducted in 17 countries had found a median CD_4 cell count increased by +170 cells/mm^3 in NVP and +190 cells/mm^3 in EFV based regimen both with the d4T/3TC backbone at 48 weeks from baseline median just below 200 cells/mm[38]. The mean CD_4^+ count change of d4T/3TC/NVP was lower than the mean CD_4 cell count of ZDV/3TC/NVP 257.27 cells/mm^3 (SD = 155.13) at 6th month from baseline mean CD_4 count 129.93 cells/mm^3 (SD = 74.72). Similar to the result of this study, the comparative study conducted in Cameroon showed the median CD_4^+ cell count in ZDV/3TC/NVP group patients were higher than in those receiving a d4T/3TC/NVP based regimen (152 V_S 117cells/mm^3)[9]. Another comparative study conducted in Australia for 52 weeks also indicated the mean increases in CD_4^+ T-cell counts in the AZT/3TC/NVP group (+139 cells/mm^3) was greater than the d4T/3TC/NVP group (+113 cells/mm^3)[10]. The mean CD_4^+ cell count recovery rate of TDF/3TC/EFV from baseline 110.06 cells/mm^3 (SD = 83.306) to 283.06 cells /mm^3 (SD = 142.03) have shown the lower immunological success than d4T/3TC/EFV at 6th month of treatment initiation. Similar comparative study conducted at 81 centers in United States, South America and Europe had found the superiority of d4T/3TC/EFV over TDF/3TC/EFV with mean CD_4 cell count increase of +283 cells/mm^3 and +263 cells/mm^3 respectively[11]. The comparative study of mean CD_4 cell count change of different types of ART treatment regimens of this study showed different outcomes of mean CD_4^+ cell count increase at 6th month of treatment initiation. The d4T/3TC/EFV

regimen showed higher mean CD_4^+ count change than ZDV/3TC/EFV regimen and compared to these EFV based regimens TDF/3TC/EFV showed lower mean CD_4^+ cell count change. The NVP based combination ZDV/3TC/NVP have better mean CD_4^+ cell count outcome than d4T/3TC/NVP regimen, but compared to EFV based regimens these have lower mean CD_4^+ cell count outcome. The EFV and NVP based combinations both with d4T/3TC backbone were the most and the least effective on mean CD_4^+ cell count increase respectively. Also the ZDV/3TC backbone EFV based regimen have more effective mean CD_4^+ cell count change than NVP based regimen combined with the same d4T/3TC backbone. Other combination TDF/3TC backbone with EFV was superior to ZDV/3TC/NVP, but inferior to ZDV/3TC/EFV. The findings of this study that was observed at the 6th month is also observed in a study conducted in Thailand where NRTIs backbone EFV based regimens resulted in better CD_4 cell count outcome than NVP based regimens with NRTIs backbone[12].

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CONCLUSION

HIV/AIDS affected the globe severely especially those in resource limited setting before the introduction of ARV drugs. Treatments with NRTIs and NNRTIs regimens are benefiting PLWHA of JUSH at different level. The mean CD_4^+ cell count recoveries of EFV and NRTIs were higher than NVP and NRTIs. The increase in mean CD_4^+ cell count was greater in ZDV/3TC/EFV than TDF/3TC/EFV, but lower than d4T/3TC/EFV. On other hand, ZDV/3TC/NVP mean CD_4^+ cell count change was greater than d4T/3TC/NVP.

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