International Journal of Research in Medical Sciences
Pandharpurkar D et al. Int J Res Med Sci. 2019 Jun;7(6):2177-2181
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20192494

Original Research Article

Clinical and immunological responses of zidovudine lamivudine-nevirapine versus tenofovir lamivudine-efavirenz antiretroviral treatment among HIV-1 infected adults: Gandhi Hospital, Telangana, India

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Received: 18 March 2019
Accepted: 03 May 2019

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ABSTRACT

Background: HAART (Highly active antiretroviral therapy) is the cornerstone of management of patients with HIV infection. Antiretroviral therapy was started in the year 1986 with the first drug Zidovudine (ZDV). Later on, other antiretroviral drugs (NRTIs, NNRTIs and Pls) were introduced. Dual and mono therapies were used initially but the problem of resistance emerged. Currently, 3 or more ARV drugs are recommended globally for the treatment of people with HIV infection.
Methods: A cross-sectional descriptive study conducted at a tertiary care Hospital over 200 patients, two commonly used medications are ZLN (Zidovudine+Lamivudine+Nevirapine) and TLE (Tenofovir+Lamivudine+Efavirenz). The factors considered to affect the clinical and immunologic outcomes in both groups were assessed using baseline CD4 count, WHO clinical staging, presence of chronic diarrhea, anemia, and baseline weight, occurrence of TB, and switching of ART regimen.
Results: A total of 200 patients were included in the study. ART documents of 100 patients are on Zidovudine+Lamivudine+Nevirapine) and 100 patients are on TLE (Tenofovir+Lamivudine+Efavirenz) regimen. Out of 200 patients, 97 were males and 103 were females. Maximum number of subjects were in the age of 15-45 years (82.5%) followed by 45 and above (17.5%). Mean age was 34.5±2.5 (years) with range 15 to 65 years. The baseline CD4 count of the patients, 94 were <350 and 6 were ≥350 on ZLN, in case of TLE 82 were <350 and 18 were ≥350. CD4 count after 6 months in 200 patients as follows, 60 were <350 and 40 were ≥350 in case of TLE 53 were <350 and 47 were ≥350.
Conclusions: This research finding concluded that there is no critical difference between the two medications in regards to serious adverse events but did find that TDF is superior to AZT in terms of immunologic response and adherence and more frequent emergence of resistance.

Keywords: Anti-retroviral drugs, CD4% count HIV, TLE, ZLN

INTRODUCTION

Patients on Antiretroviral Therapy (ART) for HIV-1 infection significantly suppress viremia, improves CD4 count and reduces overall disease progression. HAART

(Highly active antiretroviral therapy) is the cornerstone of management of patients with HIV infection. Initiation of widespread use of antiretroviral therapy marked declines in the incidence of most AIDS defining conditions and mortality both in the developed and developing world.[1,2] Antiretroviral therapy was started in the year 1986 with the first drug Zidovudine (ZDV). Later on, other antiretroviral drugs (NRTIs, NNRTIs and Pls) were introduced. Dual and mono therapies were used initially but the problem of resistance emerged. Currently, 3 or more ARV drugs are recommended globally for the treatment of people with HIV infection. Though, the use of antiretroviral therapy is not the final solution to HIV/AIDS prevention and care programs. The standard therapy consists of two Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and one non-nucleoside reverse transcriptase inhibitor (NNRTI).

Both Tenofovir and Zidovudine are ARV drugs which are commonly used in combination with other ARVs in the management of HIV infection as part of the first line regimen. Tenofovir is a nucleotide reverse transcriptase inhibitor (NtRTI). Zidovudine is an ARV which belongs to the class of nucleoside reverse transcriptase inhibitors (NRTIs).[3-5] However, both drugs are associated with side effects

Both the regimens zidovudine and tenofovir are used as first line antiretroviral treatment (ART), although zidovudine is associated with side-effects such as chronic anemia, which are likely to affect patients' QoL (Quality of life). In case of Tenofovir it has a better safety profile compared to zidovudine, with the main side-effect being renal toxicity.[6]

According to some studies tenofovir is superior to zidovudine in terms of its safety profile because of a reduced incidence of anemia and fat redistribution.[4,7-9] Some other studies revealed that Tenofovir had fewer side effects, but the range of side-effects studied was limited.[10]

There are limited data comparing ZLN (Zidovudine+Lamivudine+Nevirapine) and TLE (Tenofovir+Lamivudine+Efavirenz).

To study the clinical, immunological responses, safety and effectiveness of anti-retroviral drug regimens ZLN (Zidovudine+Lamivudine+Nevirapine) and TLE (Tenofovir+Lamivudine+Efavirenz) in tertiary care hospital.

METHODS

A cross-sectional descriptive study was conducted from January to December 2014 by reviewing ART documents of adults infected with HIV-1 who were on ART at ART Centre Gandhi Hospital.

Sample

At the time of data collection about 200 adults with HIV infection were on follow up at ART centre. The sampling procedure was determined by patients' ART regimen and to minimize sampling errors. Two commonly used medications are ZLN (Zidovudine+Lamivudine+Nevirapine) and TLE (Tenofovir+Lamivudine+Efavirenz). The factors considered to affect the clinical and immunologic outcomes in both groups were assessed using baseline CD4 count, WHO clinical staging, presence of chronic diarrhea, anemia, and baseline weight, occurrence of TB, and switching of ART regimen.

Patients were followed up after 6 months with similar procedure and above investigations were repeated.

Statistical analysis

The databases were analysed and assessed with appropriate statistical methods within different groups. Software used is SPSS-IBM version 21. Given statistical tools were employed to analyse the data obtained-Mean, Standard deviation, ANOVA, chi square test.

RESULTS

A total of 200 patients were included in the study. ART documents of 100 patients are on Zidovudine+Lamivudine+Nevirapine) and 100 patients are on TLE (Tenofovir+Lamivudine+Efavirenz) regimen.

Out of 200 patients, 97 were males and 103 were females. Maximum number of subjects were in the age of 15-45 years (82.5%) followed by 45 and above (17.5%). Mean age was 34.5±2.5 (years) with range 15 to 65 years (Table 1).

Table 1: Cross tabulation with chi-squares test showing some demographic and clinical parameter at start of ART.

Indicator		ZLN	TLE	P-Value
Gender	Male	59	38	0.002
	Female	41	62	
Age distribution	15-45	81	84	0.576
	45-above	19	16	
WHO clinical stage	I and II	90	77	0.001
	III and IV	10	33	

All 200 patients who are on ZLN and TLE based regimen were reviewed. Males constitute 48.5% (97/200) while females were 51.5% (103/200).

Clinical outcome

Patients who are on ZLN falls under WHO I and II constitutes 90 (90%) and III and IV 10(10%) where as in

TLE WHO stage I and II 77 (77%) and III and IV 23 (23%) (Table 2).

Table 2: Common side effects observed in both ZLN and TLE regimens.

Side Effects	ZLN N=80	TLE N=64
Anemia	16 (20%)	5 (8%)
Skin rash	10 (13%)	1 (2%)
Vomiting	9 (11%)	8 (13%)
Diarrhoea	7	2
Headache	5	11 (17%)
Fever	6	9
CNS side effect	5	14 (22%)
Depression	12 (15%)	4
Fatigue	4	2
Joint Pains	7	8 (13%)

Immunologic outcome (CD4+ change)

Out of 200 patients, the baseline CD4 count of the patients, 94 were <350 and 6 were ≥350 on ZLN, in case of TLE 82 were <350 and 18 were ≥350. CD4 count after 6 months in 200 patients as follows, 60 were <350 and 40 were ≥350 in case of TLE 53 were <350 and 47 were ≥350 (Table 3).

Table 3: Cross tabulation with chi-squares test showing CD4+ change at start of ART.

Base line	<350	≥350	P value
ZLN	94	6	0.009
TLE	82	18	
After 6 months	**<350**	**≥350**	**P value**
ZLN	60	40	0.31
TLE	53	47	

Side effects in both (Zidovudine+Lamivudine+Nevirapine) and TLE (Tenofovir +Lamivudine +Efavirenz) regimens

Among 200 patients common side effects were observed in 144 patients in both TLE and ZLN regimens among 200 patients. Among them, majority of patients with ZLN regimen had Skin rash, anaemic, fever, vomiting, depression, headache. And in patients with TLE regimen had drowsiness, skin rash, depression, fever, vomiting.

CD4 count comparison of ZLN and TLE regimen

CD4 count comparison of ZLN and TLE regimens was done by independent 't' test had shown there is no significant difference between the two regimens, both had equal efficacy profile during the treatment. ZLN regimen (Mean: 219.63 Std. Deviation: 150.19, Std. Error mean: 15.01) and TLE regimen (Mean: 233.16, Std. Deviation: 200.0Std. Error mean: 20.0) (Table 4).

Table 4: CD4 count comparison of ZLN and TLE regimen.

CD4 count	ZLN	TLE
N	100	100
Mean	219.63	233.16
Std. Deviation	150.19	200.0
Std. Error mean	15.01	20.0
F	0.56	
df	99	
Sig. (2 tailed) P value	0.55	
Mean difference	13.53	
Std. Error difference	5.0	
Correlation Coefficient	0.1	

DISCUSSION

The purpose of this article was to assess which of these two medications was the best for initial treatment for people living with HIV. Zidovudine+Lamivudine+Nevirapine) was the most common regimen prescribed in the ART centre which happens to be regimen I of National AIDS Control Organization (NACO) and is recommended as a first-line regimen.[11]

In this study, after 1 year of Zidovudine+Lamivudine+Nevirapine ART regimen the mean CD4 cell count was 219 ml, and 233 ml from Tenofovir+Lamivudine+Efavirenz group the mean CD4 cell with little significant difference among the two groups. Our study finding shows the activity of ZLN and TLE regimens, the combination resulted in a more sustained increase in a CD4 counts with no significant difference over the 12 months period that we took to study the cases. Several studies and clinical trials have shown that CD4 count is the strongest predictor of subsequent disease progression and survival.[12,13] Also CD4 count is critical for determining patient's disease stage and short-term and midterm risk of opportunistic infections and initiation of antiretroviral therapy. The use of the CD4 count as an independent and reliable marker for treatment outcome is striking from various aspects. First, CD4 counts are already the most important factor in deciding whether to initiate antiretroviral therapy and opportunistic prophylaxis.

On comparing incidence of clinical outcomes in the subjects during follow up period, maximum incidence was found in ZLN group i.e. (N= 80) and, in other group incidence TLE was (N=64).

On comparing incidence of opportunistic infections outcomes in the subjects during follow up period, maximum incidence was found in ZLN group i.e. (N= 80) and, in other group incidence TLE was (N=64).

Overall incidence of TB was 41.1%, in case of ZLN group N=11 (13%) and, in other group incidence TLE N=18 (28.1%).

Ayele T et al, 2017 reported that TDF based regimens especially, TDF/3TC/EFV had excellent immunologic recovery followed by AZT based NVP.[5] Since aged patients, those with baseline CD4+ count <200 cells/mm^3 and patients with pre-treatment BMI <18.5 were poor immunologic responders, they need special attention while delivering care and treatment and also observed that there is no difference in clinically, immunologically and virologically among patient taking NVP+AZT+3TC versus EFV+AZT+3TC regimen. However, the prevalence of sub-immunologic recovery among the TDF users in the resource constrained settings needs to be assessed further. Hemasri et al, has studied both ZLN and TLE regimens for treatment in HIV patients are efficacious in improving both CD4 count(p value: 0.016). Now even though the combination of ZLN is very efficacious as an anti-retroviral drug regimen, but TLE should be preferred.[14] Special attention should be paid to patient's CD4 level after this drug therapy is initiated by giving the patient regular monthly tests for CD4 estimation and supplementing the drug regimen with drugs that improve CD4. Sorsa A in 2017 studies revelled that there was no significant difference in mortality between those exposed to TDF versus AZT based regimens.[15] The proportion of death and OIs in the subgroup belonged to TDF/3TC/EFV was lower as compared to those belonged to other regimens under study although the difference was not statistically significant.

CONCLUSION

This research finding concluded that there is no critical difference between the two medications in regards to serious adverse events but did find that TDF is superior to AZT in terms of immunologic response and adherence and more frequent emergence of resistance. However, these two studies are not directly comparable because they used two related different drugs in addition to TDF and AZT. Future studies and recommendations should focus on specific toxicities and tolerability when comparing these two medications.

Funding: Funding sources from Telangana State AIDS Control Society, Hyderabad, India
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Pandharpurkar D, Gudikandula K, Mallikarjun P. Clinical and immunological responses of zidovudine lamivudine-nevirapine versus tenofovir lamivudine-efavirenz antiretroviral treatment among HIV-1 infected adults: Gandhi Hospital, Telangana, India. Int J Res Med Sci 2019;7:2177-81.