Evaluation of Efficacy of Nevirapine Regimen versus Efavirenz Regimen

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Abstract

Introduction: CD4 count can be used as marker to assess the effectiveness of antiretro viral treatment (ART), mortality and survival rates in HIV patients. It is an important guide to treatment as it reflects drug resistance, treatment failure and need to switch over to different regimen. Objective of the study was to assess the effectiveness of two regimens, Nevirapine (NVP) versus Efavirenz (EFV), both in combination with Zidovudine (AZT) and Lamivudine (3TC) in HIV patients.

Methods: A retrospective observational study on 48 adult HIV patients, receiving AZT+3TC+NPV (ZLN) (group I) and 28 patients on AZT+3TC+EFV (ZLE) (group II) was carried out. Demographic profile, medication prescribed, baseline CD4 cell counts, serially monitored CD4 count values for 2 years and Hb% were recorded from patient's medical record.Basal and 2 yr CD4 counts were compared using suitable statistical tests.

Results: A very highly significant (p=0.0001) increment in CD4 count was observed in both the groups after treatment. Mean CD4 count of 2 years was significantly high (p=0.038) in patients on EFV regimen as compared to those on NVP.

Conclusion: We conclude that ART regimen containing EFV is superior to NVP. However further studies need to be done in this area, by taking adherence to treatment, concomitant infections, ADRs in to consideration.

Key words: CD4 Count, Efavirenz, Nevirapine.

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Introduction

Acquired immune deficiency syndrome (AIDS)-related morbidity and mortality have been reduced significantly by the use of highly active antiretroviral therapy (HAART). Access to antiretroviral therapy (ART) has improved tremendously over the last few years due to implementation and enforcement of various strategies by National AIDS Control Organization (NACO) in India. NACO has established ART centers in selected government hospitals which offer free treatment for HIV/AIDS and related opportunistic infections[(1)]. In India NACO offers systematic HIV care by providing drugs free of cost, a counseling algorithm in detail for psychosocial support and management of adverse reactions, with a special emphasis on adherence to ART.

Non-nucleoside reverse transcriptase inhibitor (NNRTI)-based antiretroviral therapy (ART) is the most affordable regimen for HIV patients in developing countries. World Health Organization (WHO) recommends a combination therapy of either efavirenz (EFV) or nevirapine (NVP), both NNRTIs, with nucleoside reverse transcriptase inhibitors (NRTI) in resource-limited countries[(2)]. Studies have reported that, NVP and EFV have comparable virologic and clinical efficacy[(3-5)].

From resource limited settings, data of comparison between NVP to EFV durability among HIV infected patients is available[(3,6)]. However limited number of such studies have been done in Indian settings.

This study was conducted to evaluate the effectiveness of Nevirapine (NVP) versus Efavirenz (EFV), both are given in combination with Zidovudine and Lamivudine (3TC) in HIV-infected patients. Basal CD4 counts and CD4 count at 2 yrs as well as mean CD4 count of 2 yrs are used as tools to compare the regimens. Hence this study was designed in a teaching hospital attached to a medical college in coastal Karnataka.

Methodology

A retrospective observational study on 48 adult HIV patients, receiving AZT+3TC+NPV (group I) and 28 patients on AZT+3TC+EFV (group II) was carried out in Karwar Institute of Medical Sciences, Karwar. Data of patients who were diagnosed to be HIV positive, receiving HAART and were attending the hospital for regular follow up once in six months was collected. Patients receiving above mentioned regimens at least for two years were included and those with lesser than that period were excluded. Patients were evaluated in detail by measuring CD4 count by serially monitoring CD4 counts once in 6 months for two years. Hemogram and other laboratory parameters were also noted.

Data Collection

Data was extracted from Patient's medical records using 'white card', a data collection form designed by

NACO. Patient demography such as age, gender, medication prescribed (drug regimen), baseline CD4 cell counts, and serially monitored CD4 count values (once in 6 months) were recorded.

Patients in group I were in the age group of 39.02±1.14 years and consisted of 68.75% males and 31.25% females. They were receiving a standard drug dosages of AZT 300 mg twice daily, 3TC 150 mg twice daily or 300 mg once daily, NVP 200 mg once daily for a 2-week lead-in period and then as 200 mg twice daily.

Group II had patients in the age group of 38.79±1.33 years, 50% of them being males and 50% females. They were on a standard drug dosages, AZT 300 mg twice daily, 3TC150 mg twice daily or 300 mg once daily and EFV 600 mg once daily.

In this study we assessed the effectiveness of NVP versus EFV. Basal CD4 count and improvements in CD4 counts in subsequent follow up visits being the tool to compare and measure the effectiveness of the two regimens. Flow cytometric method was used to measure CD4 count. Patients of both the groups were staged as per WHO clinical staging guidelines, at the end of 2 yrs of treatment (Table 2).

Statistical analysis was done by using Graph pad Instat software. Student's paired 't' test was used to compare CD4 counts before and after treatment in individual groups. Unpaired 't' test was used for the comparison of CD4 counts as well as its extent of elevation between the groups. Statistical significance was fixed at level 0.05.

Results

Basal CD4 count was 250.38±19.72 cells/cmm in group I and they had a follow up count of 538.89±41.7 at the end of 2 yrs. result being expressed as mean±standard error of mean. Patients in group II had basal CD4 count of 251.36±36.08 and CD4 count of 524.7±51.77 at two years. A very highly significant (p=0.0001) increment in CD4 count was observed in both the groups after treatment. But CD4 counts did not differ significantly at the end of 2 years. However when mean of all follow up counts was considered, mean CD4 count in group II was significantly higher (p=0.038) (Table 1).

Table 1:CD4 Count in two antiretroviral regimens

	Group I (N=48) Mean ±SEM	Group II (N=28) Mean ±SEM	P value
Basal CD4 count	250.38±19.72	251.36±36.08	Not significant
CD4 count at 2 yrs	538.89±41.7	524.7±51.77	Not significant
Mean of CD4 counts of 2yrs	464.54±36.39	479.35±52.45	0.038*

*significant

Table 2: Showing WHO clinical staging of HIV patients on treatment

Clinical stage	CD4 count cells/cmm	% of patients at the end of 2 yrs	
		Group I	GroupII
I	>1200	6.26	3.57
II	500-1200	39.58	42.86
III	200-500	52.08	39.29
IV	<200	2.08	14.28
V	<50	0	0

Discussion

Improvements in CD4 counts were highly significant (p=0.0001) in both the groups (basal CD4 versus CD4 count at 2 yr). We found that there was no significant difference in CD4 counts at the end of two yrs between the groups. Extent of elevation of CD4 count was also statistically insignificant between the groups. (2.15 times in group I versus 2.09 times in group II).

Higher percentage of patients receiving AZT+3TC+NPV were distributed in stage I and III. Whereas in stage II and IV, patients on AZT + 3TC + EFV were more (Table 2). We cannot conclude from this data that, patients with which regimen are better staged. Small sample size is the limitation of our study.

Mean CD4 count of 2 years was significantly (0.038) higher in patients receivin AZT+3TC+EFV as compared to AZT+3TC+NVP. This shows the superiority of efavirenz as compared to nevirapine.

Literature suggests that EFV has shown to be superior to NVP[7-9] which support our finding. NVP is the most widely available, affordable and convenient NNRTI in low- and middle-income countries. So most of the studies in resource limited settings have focused on comparing EFV versus NVP. Compared to NVP, EFV shows a slight benefit in terms of toxicity and adverse drug reactions. Zara et al reported that EFV is associated with a lower frequency of severe adverse events, treatment discontinuations as compared to NVP[10].

Biotransformation pathways of NVP are more sensitive to induction than those of efavirenz, and nevirapine-based regimens therefore have a greater risk of subtherapeutic concentrations[11-14].

Concomitant use of NVP with rifampicin containing TB treatment is contra-indicated as there is a potential of drug-drug interactions and increased toxicity[2]. Use of EFV as the preferred NNRTI over NVP in settings where TB is endemic may result in improved first-line regimen durability. WHO guidelines recommend efavirenz rather than nevirapine for patient's co infected with HIV and tuberculosis[2]. Moreover the use of efavirenz compared with nevirapine as initial antiretroviral treatment was associated with less virological failure[15].

However controversial reports exist. A study by Sinha et al showed no significant difference in outcome, irrespective of whether efavirenz or nevirapine was used[16]. Therefore, he suggested that nevirapine based ART could be an alternative in the resource limited settings in patients with HIV and tuberculosis co-infection.

Even though EFV is proved to be beneficial over NVP, effectiveness of the treatment depends on various factors like associated co -infections, co-morbid conditions, adverse drug reactions, poor drug compliance, poor drug adherence etc. Concomitant medications have a vital role in determining the effectiveness of the regimen.

Several studies have reported that 25% of patients discontinue initial HAART regimen because of treatment failure, toxic effects or noncompliance within the first eight months of therapy[17,18]. We could have thrown more light on this had we considered treatment adherence into account.

Conclusion

We conclude that ART regimen containing AZT/3TC/EFV is proved to be superior to that containing AZT/3TC/NVP. However further studies need to be done in this area, by taking adherence to treatment, concomitant infections, adverse reactions which lead to poor drug compliance in a larger population of patients to explore more information.

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Conflict of Interest: None

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