

CD4 Change among HIV Patients on ART Regime, Switch Over from Nevirapine to Efavirenz: A Comparative Study

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ABSTRACT

Introduction: Annual incidence of HIV infection in India is about 1.16 lakh among adult population in 2014. This study has been conducted to compare immunological outcome and effect on liver function by either Nevirapine (NVP) containing regime that is ZLN (Zidovudine, Lamivudine, Nevirapine) or Efavirenz (EFV) containing regime that is TLE (Tenofovir, Lamivudine, Efavirenz).

Material and Methods: The study was conducted at a tertiary care centre over 105 patients this study was an observational study. The patients were evenly matched and categorized in three groups, Group A (ZLN), Group B (TLE), Group C (ZLN to TLE) and these patients received three antiretroviral drug one of the drug was either nevirapine (NVP) or efavirenz (EFV). Patients were followed up for 6 months for any change in CD4 count.

Result: All subjects (i.e. 105) were followed for 6 months. Initially base line CD4 count has significant difference among each group and the difference in CD4 count after 6 months of therapy was also significant. Rise in CD4 count seen in each group but significant rise ($p < 0.05$) in CD4 count seen among group B and C only i.e. who were taking TLE and or change their regime from ZLN to TLE respectively. The average rise in CD4 count was 18.2, 103.4, 108.6 in group A, B, C respectively. After 6 month of therapy there was a significant difference ($p < 0.05$) in CD4 count when all three groups were compared.

Conclusion: The antiretroviral regimen containing EFV was associated with better immunological outcome, than NVP containing regimen

Keywords: Nevirapine, Efavirenz, Opportunistic infections, ZLN and TLE Regime

INTRODUCTION

The most of new infections is found in six high prevalence states which is account for 31% of all new infections and ten low prevalence states account for 57%¹ and remaining 12% incidence found in rest thirteen states. In 2014 estimated population of people living with HIV (PLHIV) was around 21 lakhs. During initial care of HIV- positive patient the initiation of type of regimen is an important thing, so Ideal initial regimens are that which ones are effective, well tolerated and which look into various biochemical, physical and economical aspects of the patients. Most of the Clinical guidelines generally recommend regimens consisting of two nucleoside reverse transcriptase inhibitors (NRTIs) and one non-nucleoside reverse transcriptase inhibitors (NNRTI). According to WHO ART regime should consist of a NRTI backbone with either nevirapine or efavirenz.² According to BHIVA (British HIV Association) and EACS (European

AIDS Clinical Society) recommendations both efavirenz and nevirapine are effective and either of them can be used but these guidelines specify the conditions where one of these can be preferred or used.^{3,4} A pooled analysis of randomized clinical trials comparing efavirenz and nevirapine suggested a higher survival rate for efavirenz.⁵

There are many NNRTIs but now a days two NNRTIs NVP and EFV available for clinical use for management of HIV in india. For initiation of ART most of the time EFV has been recommended as first line NNRTI and NVP as an alternative NNRTI. As the cost of NVP is lesser than that of EFV so in resource poor country like Indian subcontinent country and African country WHO has recommended NVP as one of the first line NNRTI for initiation of ART. The patients who are taking an efavirenz containing regimen had better virologic outcomes⁶⁻¹², also better immunologic responses^{6,7}, and lesser chances of acquiring various OI's than those who were taking a nevirapine as initial ART regime. Study aimed to compare regimen containing either of nevirapine or efavirenz and two or more NRTI among HIV infected patient in respect to immunological outcome.

MATERIAL AND METHODS

This study was an observational study and was conducted on 105 subjects for the duration of 1 year and 4 months, from March 2015 to July 2016 in tertiary care centre i.e. MLN Medical college and its associated SRN Hospital Allahabad. The cases were selected on the basis of inclusion criteria and there were no control group in this study.

Procedure

Subjects for the study were taken from admitted patients from PG department of medicine MLN Medical college Allahabad, Patients visiting ART Centre or OPD in Department of Medicine, MLN Medical College for ART treatment. All subjects were divided into 3 groups viz. Group A (ZLN), group B (TLE), and group C (ZLN to TLE).

The duration of study was around one and half year and follow up of the patients was done after 6 months as patients generally visited at 6 month for his or her CD4 count so in

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| Regime(Group) | Baseline CD4 count (cell/ μ l) | CD4 Count after 6 month (cells/ μ l) | Average increase in CD4 count | P value |
|-------------------------------|------------------------------------|--|-------------------------------|---------|
| ZLN (Grp A) | 307.9 \pm 56.8 | 326.1 \pm 63.6 | 18.2 \pm 6.8 | 0.41 |
| TLE (Grp B) | 290.2 \pm 58.1 | 393.6 \pm 76.5 | 103.4 \pm 18.4 | 0.001 |
| ZLN \rightarrow TLE (Grp C) | 258.1 \pm 59.6 | 366.7 \pm 63.2 | 108.6 \pm 3.6 | 0.001 |

Table-1: CD4 Count before and after treatment

| Regime(Group) | Baseline Hb conc. (gm/dl) | Hb conc. After 6 month | P value |
|-------------------------------|---------------------------|------------------------|---------|
| ZLN (Grp A) | 10.4 \pm 1.3 | 9.4 \pm 1.1 | 0.002 |
| TLE (Grp B) | 10.3 \pm 1.3 | 10.1 \pm 1.2 | 0.11 |
| ZLN \rightarrow TLE (Grp C) | 8.6 \pm 1.3 | 10.2 \pm 1.3 | 0.003 |

Table-2: Effect of therapy on Hemoglobin concentration

this study 6 month of follow up period were taken, procedure was similar to follow up the patients at first visit and after 6 month. At first visit patients the noted investigations were done like CD4 (cluster of differentiation 4) cells count, Liver function tests (SGOT/SGPT), Complete blood count(CBC), serum electrolytes, serum urea and creatinine, and Chest x-ray (postero-anterior view). Similar investigations were repeated after 6 months. At 6 month enquiry was done about health status of the patient main focus was if the patients had any history of OI's during this time and also asked about patients compliant toward ART. It was ensure that for whole of the 6 months period patient remained on same regime of ART, if there was change in the regime by any reason subjects were exempted from study.

Inclusion criteria

- Young adult (> 18 years).
- Patients who are taking ART containing either NVP or EFV and registered in ART centre of MLN Medical college.

Exclusion criteria

- Pregnant patients.
- Patient on ART not containing either NVP or EFV.

STATISTICAL ANALYSIS

The appropriate statistical method were used during analyzing databases like Mean, Standard deviation, ANOVA, Paired 't' test and for analyzing data between different groups by using software SPSS-IBM version 21.

RESULTS

Most of the patients were male i.e. 65 and lesser were female i.e. 40. In this study maximum incidence of HIV were found among 30-40 years of age group (61.9%) followed by 40-50 years age group (29.5%). Range of age was from 26 to 52 years with mean 37.2 \pm 5.7 years. Highest number of patients were among group A followed by group B and least number of patients was in group C.

CD4 count

Initially base line CD4 count has significant difference among each group, there was significant rise (p value <0.05) in CD4 count among group B and C i.e. who were taking TLE and or change their regime from ZLN to TLE respectively and

there was also rise in CD4 count who were taking ZLN, but the number was not significant (p>0.05).

The average rise in CD4 count was 18.2, 103.4, 108.6 in group A, B, C respectively. After 6 month of therapy there was a significant difference (p< 0.05) in CD4 count when we compare all three groups.

After applying paired t test it was found that there was increase in CD4 count seen in all three group, maximum rise in CD4 count is seen with patients who shifted from ZLN to TLE i.e. 108.6 cells/ μ l, which is a significant no.(p = 0.001). While minimum increase in CD4 count i.e. 18.2 cell/ μ l seen in patients taking ZLN which is insignificant (p>0.05). The patients who were started on TLE they also shows significant increase in CD4 count i.e. 103.4 cells/ul (p<0.05) (Table 1).

Effect of therapy on Hemoglobin (Hb) concentration

Patients who were taking ZLN shows significant (P<0.05) decrease in hemoglobin concentration during the course of 6 month and there were decrease in approximately 1 gm% of Hb. Patients who were taking TLE shows slight decrease in Hb (0.2gm%) which is not significant at all, while patients whose regime were changed(ZLN to TLE) they shows a significant increase in Hb (1.6gm%) concentration.

DISCUSSION

In this observational cohort study, maximum number of the subjects belong to the age group 30-40 yrs followed by >40 yrs age group. Majority of subjects were males and most of them were young adult so it can be predicted that prevalence of HIV is more in young adult male.

Efavirenz based HAART is current standard of care in management of HIV infected patients with long term efficacy data are available. In developing country like India nevirapine based HAART is cheap compared to efavirenz based HAART.

Efficacy and safety of Nevirapine based HAART had also been demonstrated in various study. In this study we found that HIV infected patients had better immunological outcome who are taking Efavirenz based HAART (TLE) than the patients taking Nevirapine based HAART (ZLN).

The immunological response in this study is indicated by CD4 count. It was found that the average rise in CD4 count in patients on Nevirapine based regime (ZLN) was merely 18.2 cells/ μ l (SD=6.8) which is insignificant (p=0.412) while the patients who was taking Efavirenz based regime (TLE), the average increase in CD4 count was 103.4 cells/ μ l (SD=18.4) and in patients who change from ZLN to TLE rise in CD4 count found to be 108.6 cells/ μ l(SD=3.6),this is marginally greater than previous group.The p value in both the group is 0.001 which is significant, this shows that EFV containing HAART has better immunological outcome than

NVP containing HAART.

In SENC¹⁴ (Spanish efavirenz vs. nevirapine comparison) trial, I.Co.N.A.¹⁵ (Italian cohort naïve antiretroviral) and AK Patel, S Pujari et al¹⁶ study immunologic response was nearly same in NVP and EFV arms. Manfredi et al found immunological advantage of EFV over NVP.

Alessandro Cozzi-Lepri, Andrew N. Phillips et al⁹ in a study compared immunological and virological response to regime containing either of EFV or NVP and found that the rise in CD4 count were more among the patients who were taking EFV containing regime and there was also less incidence of virological failure among these patients.

There is low frequency of anemia seen with TLE based HAART while there is increase in hemoglobin concentration seen with group C (ZLN→TLE) patients. This type of result most probably due to Zidovudine induced anemia it is nothing to do with either with NVP or EFV. In group C whose regime was changed in most of the cases reason was Zidovudine induced anemia.

CONCLUSION

Prevalence of HIV was more among age group 30-40 years and its incidence is also increasing in younger population. Prevalence was more common in males than females and most common route of transmission was found to be heterosexual contact. Efavirenz based regime had better immunological outcome than Nevirapine based regime. EFV based regime had better compliance and adherence to therapy probably because of lesser side effect profile than NVP based regime.

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