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Original Research Article

The effect of nevirapine vs efavirenz containing regimens on clinical outcomes among HIV patients on ART: a comparative study

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ABSTRACT

Background: The present study has been conducted to compare regimens containing either of nevirapine (NVP) and efavirenz (EFV) and two or more nucleoside reverse transcriptase inhibitors (NRTIs) among HIV infected patients in respect to clinical outcome and to compare incidence of opportunistic infections among these patients.
Methods: This study was an observational study conducted at a tertiary care centre over 105 patients, who were evenly matched and received three antiretroviral drug one of the drug was either nevirapine (NVP) or efavirenz (EFV) and these patients were followed up for 6 months for occurrence of any opportunistic infections during these 6 months.
Results: 105 patients were followed for 6 months, the maximum incidence of opportunistic infection (OI's) was found among patients who were on ZLN (zidovudine, lamivudine, nevirapine) regime i.e. 60% followed by patients who changed their regime from ZLN to TLE i.e. 36.5%, while the least incidence of OI's was noted among the patients who were on TLE (tenofovir, lamivudine, efavirenz) regime i.e. 28.5%. These differences were found to be statistically significant ($p<0.05$).
Conclusions: EFV containing antiretroviral regimen was associated with superior clinical outcome than NVP containing regimen.

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

INTRODUCTION

Annual incidence of HIV infection in India is about 1.16 lakh among adult population in 2014.[1] The six high prevalence states account for only 31% of new infections, while the ten low prevalence states account for 57%.[1] The total number of people living with HIV (PLHIV) in India is estimated around 21 lakhs in 2014.The choice of initial antiretroviral regimen is an important component of the care of HIV-positive patient. Ideal initial regimens are the ones that are well tolerated, effective and which take into account various physical and biochemical parameter of the patient. Clinical guidelines generally include regimens consisting of one non-nucleoside reverse transcriptase inhibitors (NNRTI) with two nucleoside reverse transcriptase inhibitors (NRTI)s.

The WHO recommends regimens consisting of a NRTI backbone with either efavirenz or nevirapine[2]. The European AIDS Clinical Society (EACS) and British HIV Association (BHIVA) guidelines also recommend both efavirenz and nevirapine, but specify the conditions where either of these can be preferred.[3,4] A pooled analysis of randomized clinical trials comparing efavirenz

and nevirapine suggested a higher survival rate for efavirenz.[5] At present EFV and NVP are two NNRTIs available for clinical use in management of HIV. EFV has been recommended as one of the first drug of choice and NVP as an alternative agent for initiation of ART. In resource poor setting WHO has recommended NVP as one of the first drug of choice for initiation of ART. Those taking an efavirenz containing regimen had better immunologic responses, better virologic outcomes and were less likely to develop poor clinical outcomes than those taking a nevirapine containing regimen.[6-13]

METHODS

Study design

This observational study was conducted over 105 subjects at MLN Medical College and associated SRN Hospital, Allahabad, Uttar Pradesh, India during a period from March 2015 to July 2016. Cases were selected according to inclusion criteria and there was no separate control group for the study.

Procedure

This study was conducted on patients attending ART Centre in Department of Medicine, MLN Medical College for ART treatment, or admitted in the department of Medicine. Subjects were divided into 3 groups viz. group A (ZLN), group B (TLE), and group C (ZLN to TLE). A detailed history was taken and thorough clinical examination and relevant investigations were done in each subject to assess present health status of the patients. History included duration of HIV infection, present complaints, any treatment being taken along with ART or any concurrent or chronic illness. Base line investigation was done- CD4 (cluster of differentiation 4) cells count, complete blood count, liver function tests (SGOT/SGPT), serum urea and creatinine, serum electrolytes and chest x-ray (Posterio-anterior view).

After 6 months these patients were followed up with similar procedure and above investigations were repeated. In history, focus was given on development of opportunistic infections, type and number (one or many) of opportunistic infections, duration of illness, number of hospitalization needed, relapse of illness and if patient got admitted in past 6 months then for how many days he/she remain admitted.

Inclusion criteria

- Age greater than 18 years
- Patients registered at ART centre in Department of medicine M.L.N. Medical College, and who are on ART regime containing EFV or NVP.

Exclusion criteria

- Pregnant patients
- Patient on ART not containing either of NVP and EFV
- Patient not tolerating EFV containing regime.

Statistical analysis

The databases were analyzed and assessed with appropriate statistical methods within different groups. Software used is SPSS-IBM version 21. Given statistical tools were employed to analyze the data obtained- Mean, Standard deviation, ANOVA, Paired 't' test.

RESULTS

Out of 105 subjects, 65 were males and 40 were females. Maximum number of subjects were in the of 30-40 years age group (61.9%) followed by 40-50 years (29.5%). Mean age was 37.2±5.7 (years) with range 26 to 52 years. The maximum number of patients were in the ZLN taking group (Grp A) followed by patients taking TLE (Grp B) and least number of patients were in that group where patients had switched from ZLN to TLE regime (Grp C).

Opportunistic infections (OI's)

Maximum incidence of opportunistic infection was recorded among patients who were on ZLN regime i.e. 60%, followed by patients who switched from ZLN to TLE regime (36.5%), while the least incidence of OI's were noted among the patients who were taking TLE regime (28.5%); the difference of the incidence of opportunistic infections among these groups was statistically significant ($p<0.05$) (Table 1).

Table 1: Incidence of opportunistic infections.

Regime(Grp)	No. of patients (n)	No. of patients developing OI's	Percentage (%)	P-value
ZLN (Grp A)	40	24	60%	0.03
TLE (Grp B)	35	10	28.5%	
ZLN→TLE (Grp C)	30	11	36.6%	
Total	105	45	42.8%	

Type of opportunistic infections

The most common OI's among each group was pulmonary TB; overall incidence of TB was 47.1%, followed by acute gastroenteritis 24.4% while the second most common OI's in group B (TLE) was oral candidiasis while in other two groups the second most common OI's was Acute gastroenteritis (Table 2).

Table 2: Type of opportunistic infections.

Group	Pulmonary TB	Oral candidiasis	Acute gastroenteritis	Others
A	11 (45.8%)	5 (21%)	6 (25%)	2 (8.3%)
B	2 (50%)	2 (20%)	3 (30%)	Nil
C	5 (45.5%)	3 (27.2%)	2 (18.2%)	1 (9%)
Total	21 (47.1%)	10 (22.7%)	11 (24.4%)	3 (5.7%)

Table 3: Hospital admission (during course of 6 months).

Group	1 admission	2 admissions	>2 admissions	Total
A	9 (22.5%)	2 (5%)	1 (2.5%)	12 (33.3%)
B	6 (17.1%)	1 (2.8%)	Nil	7 (20%)
C	8 (26.6%)	2 (6.6%)	1 (3.3%)	11 (36.6%)
Total	23 (76.6%)	5 (16.6%)	2 (6.6%)	30 (35%)

Hospital admission and duration of hospital stay

Maximum hospital admission rate was recorded in group C (ZLN to TLE) i.e. 36.6% while minimum hospital admission rate was in group B (TLE) i.e. 20%, maximum number of patients got admitted for single time and those who got admitted, most of them were admitted for less than 5 days. Only in group A, 3 (25%) patients were admitted for more than 5 days (Tables 3 and 4).

Table 4: Duration of hospital stay.

Group	≤ 5 Days	>5 Days
A	9 (75%)	3 (25%)
B	7 (100%)	Nil
C	11 (100%)	Nil
Total	27 (90%)	3 (10%)

DISCUSSION

In this observational study, maximum number of the subjects belonged to the age group 30-40 years followed by >40 years age group. Majority of subjects were males and by this it can be predicted that prevalence of AIDS is more among males than females and also prevalence is more among young adults.

Efavirenz based highly active anti-retroviral therapy (HAART) is current standard of care in management of HIV infected patients with long term efficacy data available. But in developing countries like India nevirapine based HAART is cheaper compared to the efavirenz based HAART. Efficacy and safety of nevirapine based HAART have also been demonstrated in various studies.[14] In present study it has been found that HIV infected patients taking efavirenz based HAART (TLE) had better clinical outcome than those taking nevirapine based HAART (ZLN).

On comparing incidence of opportunistic infections in the subjects during follow up period, maximum incidence was found in NVP group (Group A) i.e. 60% and, in other group incidence was 36.6% (Group C) and 28.5% (Group C). Overall most common OI's was pulmonary tuberculosis (TB) and also in each group separately, hence type of regime does not show any association with type of OI.

Ghate M et al in their study found that tuberculosis was the most common OI with an incidence of 15.4 (95% CI 12.2-19.2) per 100 person-years, followed by oral candidiasis 11.3 (95% CI 8.6-14.5), herpes zoster 10.1 (95% CI 7.6-13.1), and cryptococcal meningitis 1.7 (95% CI 0.8-3.1) per 100 person-years.[15] In another study, Saurabh et al found the same order of incidence with TB at the top of all the OI's.

In recent data by NACO (2014), 65% cases of tuberculosis, 57.5% of candidiasis, 36% of cryptosporidiosis, 14% *Herpes zoster*, 13% PCP, 9% bacterial pneumonia, 9% cryptococcal meningitis, 3.8% toxoplasmosis and Kaposi sarcoma 0.17% have been found in India.[1] Cain L in his study found lower mortality, lower incidence of AIDS defining illness, a larger 12 month increase in CD4 count and a smaller risk of virological failure for efavirenz compared to nevirapine.[16] Libre et al in their study found no difference in mortality or AIDS defining illness in patients taking NVP and EFV based HAART while EFV and NVP had

similar median increase in CD4 count.[17] Hospital admission rate was maximum among group C patients i.e. 36.6% while minimum admission rate was seen in group B patients. Duration of hospital stay was more in group A suggesting late recovery of disease.

CONCLUSION

So based on above observations it can be concluded that EFV based HAART has better clinical outcome and early recovery than NVP based HAART and this may be because of increase in CD4 count.

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Ethical approval: The study was approved by the institutional ethics committee

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