

ORIGINAL ARTICLE

Prevalence of adherence, adverse effect and response of Anti Retroviral Therapy on People living with HIV in a programmatic setting - A Retrospective study

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ABSTRACT

Background and objective: With the advent of Anti retroviral Therapy (ART), HIV is now regarded as a chronic manageable disease. But adherence of more than 95% is essential for around 80% efficacy. Also the various side effect of the ART need to be addressed in order to increase its response. This study was done with objective to determine the response of treatment offered to patients in a programmatic setting.

Methods: A retrospective study was done in Anti Retroviral Treatment (ART) Centre, S.S. Hospital, Banaras Hindu University, Varanasi in which all patient between 18 to 55 years of age registered between March 2006 to March 2007 were taken and response to therapy, adverse effects and adherence were seen at 12 months of therapy by going through records. Patients were divided into two groups based on drugs. Group I had patients on Zidovudine based regimen and Group II consisted of patients on Stavudine based regimen. Patient already on antiretroviral drugs at the time of enrollment to ART center and pregnant females were excluded in the study.

Results: Out of 946 patients, 210(22.3%) of patients were lost to follow-up and 54(5.7%) patients expired. The mean CD4 count significantly improved with level of 98.48 ± 60.55 / μ l at the start of therapy and 379.62 ± 185.37 / μ l at 12 months ($p < 0.005$). Among the adverse side effect, the most common was zidovudine induced anemia (23.4%). Overall adherence of $>95\%$ in 76.5% patients.

Conclusion: ART is effective in a programmatic setting provided adherence is adequate. Also, monitoring for side effects of ART should be done which is one of the limiting factors of decrease adherence.

Introduction

Development of new Antiretroviral drugs and treatment regimens has made HIV now as a chronic manageable disease. Although, antiretroviral therapy does not cure HIV infection, the decrease in viral load and improvement in immunological status brought about by these drugs have resulted in marked decrease in mortality and morbidity associated with this disease.

There is sufficient evidence to prove that CD4 count can be recognized as one of the most important predictors

of HIV infection progression. It predicts development of opportunistic infection and has been shown to be a surrogate marker for determining the need of antiretroviral therapy as well as measuring the response of therapy.^[1-7]

After CD4 count antiretroviral adherence is the second strongest predictor of progression to AIDS and death.^[8-10] For any chronic disease like hypertension, 80% adherence is enough to achieve therapeutic goals but for ART more than 95% adherence is required for ART to be around 81% effective. So high level of adherence required for successful

long-term virologic suppression which has been shown in various trials.^[11-14] The adverse effect of ART can range from minor to serious adverse event. Therefore, proper monitoring of these adverse events should be done at every visit to the ART centre.

This study was done retrospectively to know the response to therapy in a cohort of patients in one year follow up in a programmatic setting.

Material and Methods

A retrospective study was done at ART Centre, S.S. Hospital, BHU, Varanasi in which treatment naïve patients between 18 to 55 years of age registered between March 2006 to March 2007 were taken and response to therapy were seen at 12 months of therapy. Patients were divided into two groups based on drugs regimen. Group I had patients on Zidovudine based regimen consisting of Zidovudine, lamivudine and 1 Non Nucleoside reverse transcriptase inhibitor (NNRTI-nevirapine/efavirenz) and Group II consisted of stavudine based regimen that is; Stavudine, lamivudine and 1 NNRTI (nevirapine/efavirenz). Patient already on antiretroviral drugs at the time of enrollment to ART center and pregnant females were excluded in the study. Patient's whose therapy was changed during the follow up were excluded from the analysis.

The patient data was collected from the patient follow up records at the ART center BHU. The response of therapy was seen in the form of mean change in CD4 count at 12 months.. Adherence were noted by the adherence record from the follow up records of the patients at the ART center. Also, the adverse effects of drugs monitored at each visit to the ART center were also noted from the follow up records.

Statistical analysis: The data were analyzed by using SPSS -16 Version. The changes in CD4 count and stage were noted and analyzed using Student 't' test and Chi square test. A p value of <0.05 was considered to be significant.

Results

Baseline characteristics of patients are showed in Table 1. Following the exclusion criteria 946 patients were registered during March 2006 to March 2007. Out of which 698 (73.8%) were male and 248 (26.2%) were female. The mean CD4 count at start of treatment was 98.48 ± 60.55 . It increased to 288.87 ± 149.83 at six months and 379.62 ± 185.37 at twelve months. Maximum numbers of patients were in stage-3 of WHO Clinical Staging System comprising of 35.9% of total

patients. Till March 2008, 211 (22.3%) patients were lost to follow-up, 54 (5.7%) patients expired and 137 (14.5%) patients were transferred to other centers.

Table 1: Overall data of patients of retrospective study

Parameters	
Age, years (Mean \pm SD)	34.84 \pm 7.08
Sex, No. (%)	
Male	698 (73.8%)
Female	248 (26.2%)
CD4+ count	
Baseline	98.48 \pm 60.55
6 month	288.87 \pm 149.83
12 month	379.62 \pm 185.37
Stage (Baseline), No. (%)	
I	192 (20.3%)
II	204 (21.6%)
III	340 (35.9%)
IV	210 (22.2%)
Outcome, No. (%)	
On treatment	544 (57.5%)
Lost to follow up	210 (22.4%)
Expired	54 (5.7%)
Transferred out	137 (14.5%)
Adherence, No. (%)	
>95%	723 (76.5%)
85-95%	3 (0.3%)
<85%	220 (23.2%)

When the patients were divided into zidovudine and stavudine based regimes and the change in mean CD4 count was seen at 12 months, the results were comparable in both groups.

Among the adverse side effect, the most common was zidovudine induced anemia, leading to change of therapy (23.40%). Peripheral neuropathy was found in 5.5% of patients in stavudine based regimen group. Nevirapine (NVP) induced rash was present in 10(1.55%) patients, leading to change of regime. Six patients on nevirapine based regimen developed hepatotoxicity in form of raised transaminases and three patient on stavudine based regimen developed lipodystrophy.

Adherence / compliance of > 95% was present in 100% patients who are on still on treatment. But the overall

adherence taking into account the compliance of patients who expired and who were lost to follow up the > 95% adherence came out to be 76.5%.

Table 2 : Comparison between Zidovudine and stavudine based regimens excluding patients who were transferred out

Parameters	Zidovudine (n=422)	Stavudine (n=386)	Significance
Age, years (Mean \pm SD)	35.02 \pm 7.66	34.46 \pm 6.62	t=1.108 p=0.268
Sex, No. (%)			$\chi^2 = 2.161$
Male	323 (76.5%)	278 (72.0%)	p=0.142
Female	99 (23.5%)	108 (28.0%)	
CD4+ count (Baseline)	104.09 \pm 60.65	91.96 \pm 59.98	t=2.841 p=0.005
Stage (Baseline), No. (%)			$\chi^2 = 20.65$
I	106 (25.1%)	55 (14.2%)	p=0.000
II	101 (23.9%)	78 (20.2%)	
III	133 (31.5%)	158 (40.9%)	
IV	82 (19.4%)	95 (24.6%)	
Outcome, No. (%)			$\chi^2 = 6.243$
On treatment	242 (57.3%)	203 (52.6%)	p=0.100
Lost to follow up	99 (23.5%)	102 (26.4%)	
Expired	17 (4.0%)	29 (7.5%)	
Transferred out	64 (15.2%)	52 (13.5%)	
Adherence, No. (%)			$\chi^2 = 2.235$
>95%	320 (75.8%)	279 (72.5%)	p=0.327
85-95%	1 (0.2%)	0 (0%)	
<85%	101 (23.9%)	106 (27.5%)	

The mean CD4 count of patients who expired was 55.78 \pm 20.27/ μ l, which was significantly lower than mean CD4 count of 95.94 \pm 55.27/ μ l of survivors. Even there was significant difference in the WHO clinical stage between the patient who survived and those who expired. Among patients who expired 40.7% were in stage IV as compared to 21.1% of the patient who survived. This finding supports that CD4 count as well as stage (WHO clinical stage) of the disease at start of therapy are strong prognostic indicators of survival of patients.

Discussion

A major concern with scaling up of antiretroviral therapy (ART) in resource poor settings is the emergence of drug resistant viral strains due to sub-optimal adherence. Very high level of adherence (>95%) is required for ART to

be effective long term, and to prevent the emergence of resistant viral strains. In a study by A. Sharma *et al.*, in India found that although the overall adherence was high, lower level of adherence were documented among patients receiving free ART.^[15] Provision of free treatment without adequate patient preparation and adherence support may compromise the success of ART scale up programme.

Table 3: Comparison at 12 months

Parameters	Zidovudine (n=287)	Stavudine (n=233)	Significance
CD4+ count (12 month)	386.06 \pm 186.52	390.31 \pm 171.14	t=1.073 p=0.284
Stage (12 month), No. (%)			c ² = 0.389 p=0.942
I			
II	270 (94.1%)	221 (94.8%)	
III	2 (0.7%)	1 (0.4%)	
IV	7 (2.4%)	6 (2.6%)	
	8 (2.8%)	5 (2.1%)	

Table 4: Adverse effects

Adverse effect	No.
Anemia	125
Peripheral neuropathy	23
Rash	10
Lipodystrophy	3
Hepatitis	6

Table 5: Comparison of baseline mean CD4 count and stage of disease between survivors and non survivors

Parameters	Survived (n=892)	Expired (n=54)	t-value	p-value
CD4+ count	99.85 \pm 60.63	76.06 \pm 55.02	2.814	0.005
Stage, No. (%)				c ² = 0.003
I	188 (21.1%)	4 (7.4%)	14.203	
II	195 (21.9%)	9 (16.7%)		
III	321 (36.0%)	19 (35.2%)		
IV	188 (21.1%)	22 (40.7%)		

Among the side effects Zidovudine induced anemia was the most predominant side effect (23.4%). Agarwal *et al.*, in their retrospective study report a high incidence of ZDV induced anaemia in HIV infected patients from eastern part of India.. Zidovudine was initiated in 1256 of 2941 (42.7%)

patients between March 2005 to December 2007.^[16] Another retrospective south Indian study has reported a relatively lower incidence (5.4%) of anaemia due to AZT^[17].

Nevirapine (NVP) induced rash was present in 10(1.55%) patients, leading to change of regime to efavirenz based NNRTI. It was low as compared to other studies done in India. Ajay Sharma *et al.*, reported NVP-induced rash in 11.8% cases, Patel *et al.*, reported NVP-induced rash in 6.6% cases and Dey *et al.*, reported NVP-induced rash in 15.6% cases^[18-20].

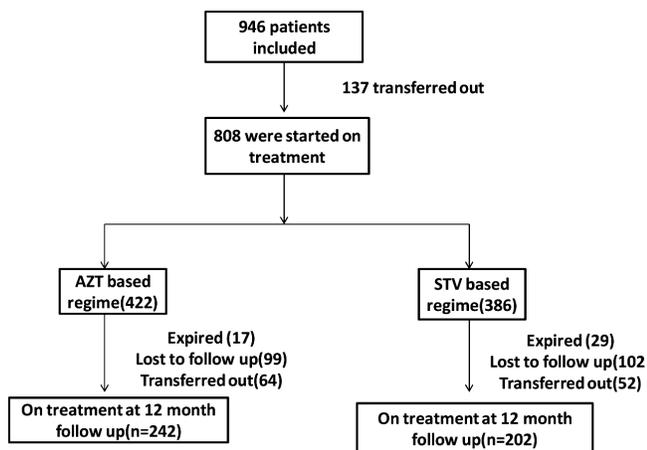


Fig. 1

Although adherence of ART is important it still remains a challenge. Adherence to ART was comparable in both groups and is one of the prognostic markers of its failure as evident by our result that those who are on treatment were having 100% compliance but when we took overall adherence taking into account those who died or those who were lost to follow up the adherence rate of <95% was present in almost one fourth of patients. Very high levels of adherence are particularly needed in developing countries like India where non-nucleoside reverse transcriptase inhibitors (NNRTI), considered as weak drugs are mostly used. Various factors like socio-demographic, stigma, cultural, economic, discrimination and factors related to health care system are proven hindrance in achieving adherence.^[21-23]

Limitation of our study included it being a retrospective study and relied on records. Because of this some adverse effect might be missed. Also it tells only about adherence by self-reporting but the cause of low adherence could not be delineated by this retrospective study.

The study however concluded that ART is effective and high compliance is needed for better outcome.

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