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Research Article

Immune Response in HIV/AIDS Patient to First Line HAART Therapy in a Tertiary Care Centre of North India

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Abstract: This study was performed in 100 patients receiving first-line highly active antiretroviral therapy (HAART) through the National AIDS Control Programme of India in May-July 2013 at ART centre PGIMS Rohtak (Haryana). The patients were followed for six month for analysing the immune response and toxicity profile of first line antiretroviral therapy. Of the 100 patients the median CD4 count of enrolled patients was 233.33±151 cells/ cumm at treatment initiation; 14% had baseline CD4 count <100 cells/ cmm. Of the 100 patients 91% were alive after 6 months. The mean CD4 count of the cohort was increased from 233.33±151 cells/cumm to 434.8 ± 217cells/cumm at six month, ($P < 0.0001$). Mean weight increased from 48.9 ± 10 Kg to 57 ± 10.7 Kg, Mean BMI increased from 22.2 ± 4 Kg/m2 to 25.9 ± 4 .3 Kg/m2 and Mean haemoglobin increased from 10.6 ± 2 gm% to 12.8 ± 1.2 gm%. The rise was statistically significant ($P < 0.0001$). The side effects of HAART were reported in 70 % of the patients. The most common toxicity reported in our study was nausea and vomiting (59 %), followed by Anemia (15 %), Hepatotoxicity (3%), and Hyper pigmenation (11 %), Neurological (8 %) Oral ulcers (10 %), Peripheral neuropathy (4%), Rash (9%). which were usually self resolving or reversed after withdrawing of the offending agents. We concluded from the study that the first line HAART is efficacious and well tolerated.

Keywords: HAART, CD4 count, NACO, ZLN, ZLE, TLE

Introduction:

The study was carried out in the Department of Medicine/A. R. T., Centre, Pt. B.D. Sharma, Post Graduate Institute of Medical Sciences, Rohtak. The study was conducted from May-July 2013. 100 patients aged more than 18 years who were eligible for the treatment according to NACO guidelines[1] were enrolled to study their immune response.. This study was a hospital based observational type study. We followed and collected data of 100 patients who were given first line HAART according to NACO guidelines at PGIMS, Rohtak.

Patients were explained about the study design and written informed consent was taken. Patient's demographic and personal details were taken. Detailed history was taken regarding presenting symptoms. A complete general and systemic examination was done at initiation and very monthly visit. Patients were given First line HAART (2 NRTI + NNRTI) therapy as per NACO guidelines. Four regimens are designated as first line HAART according to NACO which includes ZLN, TLN, ZLE and TLE. Patients were followed up for six month during this period, assessed for immune response to HAART, changes in weight, BMI, Hemoglobin, Platelets, Total Lymphocyte Counts, Blood Sugar, Lipid Profile and any possible side effects. Data was collected and analyzed by standard statistical methods.

Observations:

At the initiation of therapy, the clinical presentation of patient was as under; Fever (87%), anorexia (59%), headache (47 %), Cutaneous infection (34 %), glandular enlargement (27 %), weight loss (23%), loose motions (21%), dysphagia (16%) and cough (15%).The most common clinical finding was pallor (in 29 patients), Lymphadenopathy (in 22 patients), oral candidiasis (in 33 patients), Bronchial breathing/decreased air entry (in 9 patients). abnormal abdominal distension(in 1 patient) and neck rigidity(in 2 patient) . Many patients had opportunistic infection; most common being oral candidiasis in 33 patients, 4 patients were also found to be HBsAg positive. Tuberculosis was diagnosed in 17 patients which

included 9 patients of pulmonary, 5 patients of lymph node tuberculosis, 2 patients of CNS and 1 patient of abdominal tuberculosis .

Patients were prescribed HAART regimen according to NACO guidelines. The number of Patients prescribed ZLN was 59, prescribed ZLE was 12, prescribed TLN was 17, and prescribed TLE was 12 patients. Sixth visit 91 patients prescribed HAART amongst them ZLN was prescribed to 50 patients, ZLE was prescribed to 4 patients, TLN was prescribed to 23 patients, TLE was prescribed to 14 patients.

At initiation of study PCP (Pneumocystis carinii) prophylaxis was prescribed to 43 patients and MAC (Mycobacterium avium complex) Prophylaxis was prescribed to 8 patients. After six month of therapy CD4 count improved. Thus the number of patients who were prescribed PCP prophylaxis and MAC prophylaxis was 8 and 3 respectively.

Result and Discussion:

Out of total 100 patients, the number of patients having age less than 25 years was 22, age between 26 to 50 years was 71, and age 51 years and above was 7 patients. The study cohort was having 54 male patients and 46 female patients, 14 patients were unmarried, 86 patients were married, amongst them partners of 74 patients were also reactive. The mean age of the study cohort was 34.4 ± 10.1 years. A similar study was conducted by Bachani D *et al* [2]. In their study of 972 patients, the median age of cohort was 35 years and 66% of the patients were male. Akinboro OA et *al.;* [3] conducted similar study in 140 patients with mean age of 35.00 ± 8.8 years including 96 female patients. The study cohort was comparable except for the sex ratio and in cohort of Bachani *et al* [2] has low median CD4 count. (Table 1)

Table No. 1: Baseline characteristics in various studies.

	Present study	Bachani D [2] *et al.;*	Akinboro O.A *et al.;* [3]
Number of patients	100	972	140
Mean/median age (years)	34.4 ± 10.1	35	35.00 ± 8.8 .96
Sex ratio (M :F)	1.17: 1	2:1	1:2.2
Weight (kg)	48.9 ± 10	48.0(13.5–86)	56.79±10.22
BMI (kg/m^2)	22.2 ± 4 .3	-	20.65 ± 2.89
haemoglobin (gm%)	10.6 ± 2	10.9(1–17)	-
CD4 count (cells/cumm)	233.33±151	119(1–891)	288.36±232.23

A) Weight

In our study mean weight increased, from 48.9 ± 10 Kg to 57 ± 10.7 Kg. The increase in mean weight of cohort was 7.9 kg and it was statistically significant (P < 0.0001). In study by Bachani D *et al* [2] median baseline weight of patients was 48 kg, median weight gain was 6 kg. In the study of Akinboro O.A, *et al*[3] baseline weight of the patients was 54.05 ± 8.45 Kg and there was a rise of 6.15 kg in their study cohort. (Table I)

B) BMI

In our study the cohort's BMI increased from the baseline BMI 22.2± 4 Kg/m^2 to 25.9 ± 4.3 Kg/m^2, estimated mean rise in BMI was around 3.7 Kg/ m^2. The rise was statistically significant (P < 0.0001). Study conducted by Akinboro OA *et al.;* [3] baseline BMI of the patients was 20.65 ± 2.89 Kg/ m^2 and a mean rise of 2.34 Kg/m^2 was observed. This increase was comparable in both the studies. (Table I)

C) Haemoglobin

In present study, mean haemoglobin increased from baseline value of 10.6 ± 2 gm% to 12.8 ± 1.2 gm% with a rise of 1.1g %. The rise was statistically significant (P < 0.0001). In similar study by Bachani D *et al.;* [2] median baseline haemoglobin was 10.9 gm%. The median increase in haemoglobin was 2 g/dl which was comparable.

D) Total Lymphocyte Count

The baseline Total Lymphocyte Count was 785 ± 291 cells/cumm, which increased during six months to Total Lymphocyte Count of 862 ± 217 cells/cumm , but the rise was not statistically significant (P = 0.213). Mahajan *et al* [5] in their study of 273 patients; concluded that total lymphocyte count was a strong predictor of CD4 counts. Our result was contrary to the findings from their studies as the number of total leucocytes count has many physiological and pathological variations so they may not be significantly correlating with CD4 count.

E) CD4 count

The mean CD4 count of the cohort was increased from 233.33±151 cells/cumm at baseline to 434.8 ± 217 cells/cumm at six months (Table 2). The increase in CD4 count was of 201.1 cells /cumm as compared to baseline CD4 count and was statistically significant (P < 0.0001). The number of patients having various CD4 count less than 300 was decreased with CD4 count range of 1-99 cells/cumm from 14 to 3,

with 100-199 cells/cumm from 29 to 8 , with 200-299 cells/cumm from 32 to 10 ,and increased with CD4 count of more than 300 as in CD4 count range of 300-399 cells/cumm from 18 to 22 , 400-499 cells/cumm from 4 to 18 and ≥ 500 cells/cumm from 3 to 30. (FIGURE 1).

Study by Bachani D *et al.;* [2] median baseline median CD4 count was 119 cells/cumm, the median increase in CD4 count at 6 months after initiation of treatment was 142 cells/cumm. In similar study by Akinboro O.A et al[3], baseline mean CD4 count of the cohort was increased from 121.5±84.83 cells/cumm to 267.8±151.8 cells/cumm; the mean CD4 count increased by 144 cells /cumm (TABLE 2) .

Table No. 2 Comparative rise in Mean/Median CD4 counts.

	Present study	Bachani D *et al* [2]	Akinboro O.A *et al* [3]
Number of patients	100	972	140
Mean /median CD4 cell count (cells/cumm)	233.33±151	119	121.5 ±84.83
Increase in CD4 cell count (cells/cumm)	201.1	142	144

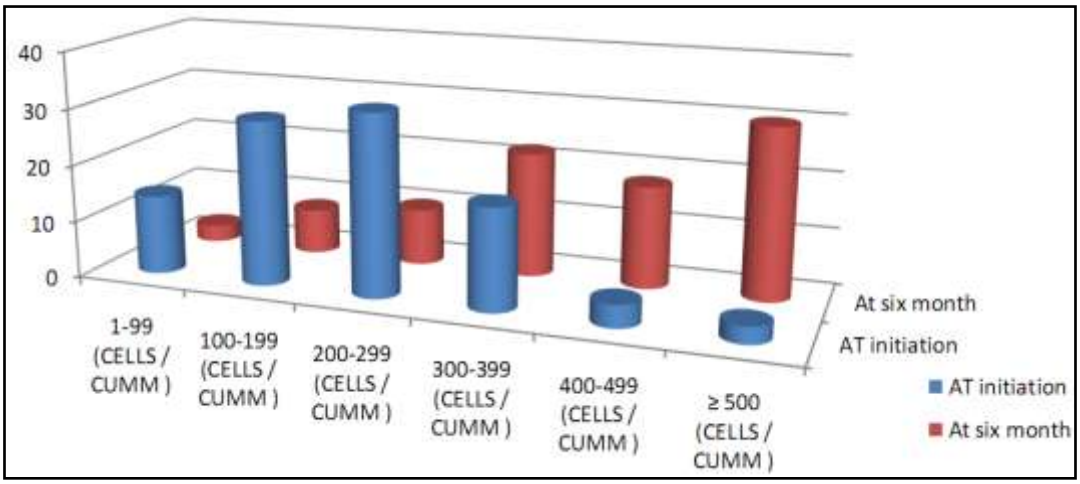

Fig-1: Showing CD4 Count Before and After Treatment

F) Toxicity Profile

Out of total hundred patients followed up for six months, 71 % patients reported at least one type of toxicity. Bachani D *et al.;* [2] showed in their study of 972 patients that 214 patients (22%) reported one or more minor or major side-effects. Sharma A[4] et al. in their study of 90 patients have reported toxicity in 71.1 % patients; while Singh H *et al.;* [6] in their study of 79 patients reported toxicity in 86% of their patients. The relative low incidence in the study by Bachani *et al.;* [2] may be due to study design as the data was retrospectively collected.

The most common toxicity reported in our study was nausea and vomiting with overall incidence of 59 % patients. Bachani D *et al.;* [2] also showed in their study that most frequent were diarrhoea and gastrointestinal adverse effects seen in 31% of the patients. Sharma A *et al.;* [4] in their study reported gastrointestinal toxicity in 11.7 % of patients while Singh H et al.[6] in their study reported gastrointestinal toxicity in 12 % of their patients. The increased incidence in our study may be attributed to increased use of Zidovudine as other studies used Stavudine as a first line regimen and it is now being withdrawn as first line agent due to the disabling peripheral neuropathy (Table 3)

Anaemia was seen in 15 % (15 /100) patients and severe anaemia grade III and IV was found in 11 (11/100) patients. Severe anaemia was also noticed as first cause of HAART regimen modification. Bachani D *et al.;* [2] had also shown in their study anaemia in 10.9 % of the patients. Sharma A *et al.;* [4] in their study reported anaemia in 32.2 % of the patients while Singh H et al. in their study, reported anaemia in 13.3 % of the patients. In some studies like our study and Sharma *et al.;* Zidovudine was used as preferred agent so incidence of anaemia was more in these studies (Table 3).

Hyper pigmentation was reported in 11 patients which includes pigmentation of skin and nail. Sharma A *et al.;* [4] also showed overall incidence of

pigmentation to be 14.4 % which was comparable in both studies (Table 3).

Skin rash was reported by 9% patients, out of them 3 patients had severe skin reaction on Nevirapine therapy and these patients were shifted to Efavirenz containing regimens of HAART regimen modification. In the study by Bachani D *et al.;* [2] skin rash was reported in 10.7 % of the patients. Sharma A *et al.;* [4] reported skin rash in 13.3 % of the patients in their study while Singh H *et al.;* [6] reported skin rash in 15.83 % of the patients (Table 3).

In our study, neurological side effects were reported in 8 %, peripheral neuropathy in 4 % and hepatitis was reported in 3 % of the patients. Bachani D *et al.;* [2] also reported in their study neurological side effects in 10 %; Sharma A *et al.;* [4] reported neurological side effects in 31.1% while Singh H et al[6]. reported neurological side effects in 4.1 %, peripheral neuropathy in 20.83 % and hepatitis in 7.5 % of the patients.

Table No. 3 Comparative incidences of toxicities in various studies

Toxicity	**Present study**	**Bachani D** *et al.;*[2]	**Sharma A** *et al.;* [4]	**Singh H** *et al.;* [6]
Total (%)	71	22	71	86
Anemia (%)	15	10.9	32.2	13.3
Hepatotoxicity (%)	3	-	-	7.5
Hyper pigmenation (%)	11	-	14.4	-
Nausea /vomiting (%)	59	31	11.7	12
Neurological (%)	8	10	31.1	4.1
Oral ulcers (%)	10	-	-	-
Pancreatitis (%)	-	-	-	-
Peripheral neuropathy (%)	4	-	-	20.83
Rash (%)	9	10.7	13.3	15.83

Conclusion:

The study showed that first line HAART therapy after six months of treatment leads to significant increase in mean weight, mean BMI, mean Haemoglobin, and mean CD4 counts. The side effects of HAART are reported in 70 % of the patients, which are usually self resolving or reversed after withdrawing of the offending agents.CD4 count raised significantly however totals lymphocyte count did not rise significantly. At initiation of study there were 38 patients in WHO clinical stage [7]. I, 36 patients in clinical stage II, 17 patients in clinical Stage III, and 9 patients in clinical stage IV, during the study one patient from stage I lost in follow up. Deaths in patients of Stage I was 1, of Stage II was 3 patients, of Stage III 2 patients and of Stage IV was 2 patients. At the end of study population was categorised in clinical stage I 51 patients, in clinical stage II 25 patients, in clinical stage III 11, and in clinical stage IV 4 patients. The study showed that first line HAART is efficacious and well tolerated.

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