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Effect of combinational non protease inhibitor ART treatment on CD4+ T lymphocyte count in AIDS patients: a study from East India

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Abstract
CD4+ T lymphocyte count measures the progression of HIV infection and hence considered as a useful tool for monitoring patients on antiretroviral (ART) treatment. Scattered data is available regarding the response to ART in terms of CD4+ counts. Therefore, present study was undertaken to analyze the effect of ART treatment on CD4+ cells in HIV serology positive patients in Manipur, an eastern state of India. 210 serology positive patients were counseled and enrolled after obtaining their consent. Patients were given ART treatment in following combinations as two nucleoside reverse transcriptase inhibitors, and a non-nucleoside reverse transcriptase inhibitor. The combinations used were Zidovudine + Lamivudine with Efavirenz or Nevirapine, and Stavudine + Lamivudine with Efavirenz or Nevirapine, depending on patient tolerance. Blood specimens were collected from each subject and were subjected to CD4+ cell count by fluorescent activated cell sorter (FACS). ART therapy results in increase of CD4+ count in 168 cases (80%) showed a mean increase in their cell count while 42 cases (20%) showed a net decrease in their cell count after a period of 6 months of treatment. The results of the present study showed that treatment with non-nucleoside reverse transcriptase inhibitor, Efavirenz or Nevirapine does not affect the cell count and need to be study in detail to find out the factors playing role in it.

Keywords: CD4+ T lymphocyte, HIV, Antiretroviral therapy, FACS

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INTRODUCTION

The epidemic of HIV infection and AIDS has raised newer challenges to clinicians for integration of clinical and laboratory data to achieve optimal patient management. The CD4+ T cell count is the standard test accepted as the best indicator for immunological competence of the patient with HIV infection [1]. Virus progressively destroys CD4+ lymphocytes, the primary target of HIV resulting in mean decline of 84-85 cells per µl per year [2-3] and a CD4+ T cell count decline by 14% per year, after HIV infection [4]. With each 5% drop from initial CD4+ T cell count, the risk of developing AIDS multiplies by 2.8 times, and with every drop of 100 cells per µl, the risk increases by 7% [5]. Therefore, the gradual loss of CD4+ T cells is used to monitor disease progression. Moreover, the present knowledge concerning the disease stage, disease progression, and initiation of therapy depend solely on count of peripheral lymphocyte subpopulation [6-7]. CD4+ lymphocyte count obtained in the initial evaluation of HIV infected patients are rechecked time to time depending upon the initial level of CD4+ count. According to revised classification of Centers for Disease Control (CDC), Atlanta, USA, HIV positive patients are divided into three categories depending upon CD4+ lymphocyte count such as category A=>500 cells per µl, category B=200-499 cells per µl, and category C=<200 cells per µl [8]. Considerable changes are occurring in AIDS scenario in Indian subcontinent. With that, therapy has also become more affordable to Indian patients because of reduced price of antiretroviral drugs [9]. Treatment with combinations of these antiretroviral drugs leads to reduction in level of viral replication in plasma with a net increase in CD4+ T cell subsets, which result in improved clinical outcome [10]. Majority of these reports are from the western countries. To the best of our knowledge, scanty information is available from Indian subcontinent. Keeping this in mind, present study was planned to assess the CD4+ T cell count in HIV patients, before and after the receipt of antiretroviral therapy (ART), and their correlation with the clinical outcome of the disease.

MATERIALS AND METHODS:

Study Participants and Place: A prospective study was carried out in the Immunology section of the Department of Microbiology, Regional Institute of Medical Sciences, Imphal, Manipur, India over a period of two years. 210 HIV serology positive individuals in the age group of 25-56 years were included in the study. The persons willing to participate in the study were enrolled after proper counseling. The protocol was explained in detail before enrolment. The Institutional Ethical Committee duly approved the study protocol and informed consent was obtained from each participant. This laboratory is a National Reference Laboratory for HIV, which participates in the External Quality Assurance Scheme (EQAS) conducted by Apex Laboratory, NARI, Pune under NACO and QASI, Canada.

HIV Serology: All the samples were also subjected to 3E/R/S for screening HIV antibodies. All 210 samples were tested for HIV antibodies positivity.

CD4+ T Cell Count: Cell count was done before the commencement of the treatment for baseline value and after 6 months during follow up visit. The samples were coded, and kept confidential. 4 ml of blood was collected and was used for HIV serology, and T lymphocyte subset counts. Cell count was done using FACS analysis. For FACS analysis, human anti CD4+ FITC labeled monoclonal antibodies (BD Pharminigen, USA) were used. Labeled cells were analyzed on BD FACS Canto™ II analyzer (BD Diagnostics, USA).

Treatment Groups: All the patients were given ART (triple drug combination antiretroviral drugs with two nucleoside reverse transcriptase inhibitors, and a non-nucleoside reverse transcriptase inhibitor). The combinations used were Zidovudine + Lamivudine with Efavirenz or Nevirapine, and Stavudine + Lamivudine with Efavirenz or Nevirapine depending on patient tolerance. Blood sample was collected from each individual and serum was used for CD4+ T cell count.

Statistical Analysis: Experiments were repeated three times to validate the reproducibility of experiments. SigmaStat 11.0 software was used to analyze the results and to calculate p values by Student's *t* test.

RESULTS

The effect of ART treatment on counts of CD4+ T cells in the study group is shown in table 1 and table 2. Out of 210 patients included in study group, 147 were males and 63 were females. The age range of study group was 25 to 56 with mean age of 35.7 years. 168 patients showed significant increase in CD4+ cell count as compared to their baseline counts. While 42 patients showed significantly reduced level of CD4+ count as compared to baseline counts ($p \leq 0.01$) (Table 1). Out of 168 patients, who showed increase in CD4+ counts, 4 were in stage A, 64 in stage B and 100 were in stage C. All patients in these groups showed increase in CD4+ cell count (Figure 1). In case of study group showing decrease in CD4+ counts, 8 individuals were in stage A,

26 in stage B and 8 were in stage C. All patients included in this group showed decrease in their CD4+ cell counts (Table 1).

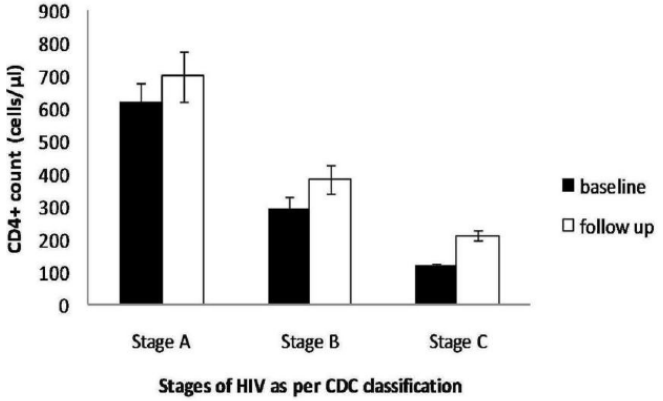

Figure 1: Figure showing the increase in CD4+ cell count of different HIV stages after ART treatment

	Effect on CD4+ T cell	No of patients	Mean CD4+ count (cells/µl) ±SD	
			Baseline	After 6 months
ART	Increase	168	195.97±124.04	289.40±144.73
	Decrease	42	285.10±153.50	236.17±127.81

Table 1: Table showing the baseline and change in mean CD4+ T cell count after ART treatment as estimated in blood samples of patients by flow cytometry

Effect on CD4+ T cell	2 NRTI +	Mean CD4+ count (cells/µl) ±SD	
		Baseline	After 6 months
Increase (n=168)	Nevirapine(n=142)	194.90±120.56	290.44±142.61
	Efavirenz(n=26)	201.81±144.08	283.69±158.69
Decrease (n=42)	Nevirapine(n=33)	289.82±159.17	243.15±129.68
	Efavirenz(n=9)	267.78±137.79	210.56±124.55

Table 2: Table showing the effect of Nevirapine and Efavirenz treatment on mean CD4+ cell count before and after 6 months of ART treatment

Out of the 210 patients included in study group, 175 patients (83.33%) received Nevirapine and 35 patients (16.67%) received Efavirenz treatment. The effect of Nevirapine versus Efavirenz treatment on the CD4+ T cell count was observed after 6 months of therapy. It was observed that both the drugs were of equal importance since significant increase and decrease in CD4+ cell count were observed in treatment with both the drugs (Table 2).

DISCUSSION

In HIV patients, the ultimate aim of antiretroviral treatment is to improve the overall clinical outcome and have been shown to reduce mortality and morbidity in patients with HIV. The goal of ART is to reduce HIV viral replication so as the CD4 count increases. However, substantial variation in CD4 count recovery has been observed. Until date, CD4+ cell count is recommended for making decision on ART [11]. In our study the benefit of ART was based on CD4+ cell count as viral load testing was not done. It was observed that, out of 210 patients, 168 showed the increase in their CD4+ cell counts while 42 patients showed decrease in their cell count from their baseline cell counts. Following ART, 168 out of 210 (80%) individuals showed an increase in their CD4+ cell count after a period of 6 months. In addition, the effect of different ART regimen showed little variation on the CD4+ T cell count. The early initiation of antiretroviral drugs does have a statistically significant effect on CD4 count especially in resource constraint countries where protease inhibitor based regimen is difficult to incorporate in the programme [12]. In the present study, infants were not included because of high variation in their cell count. Diurnal variations were also avoided by collecting samples at a specified time of the day [13]. Moreover, the factors that determine CD4+ count responses are known partly and depend on both the host and the virus, and there is substantial variation in CD4+ count recovery. The benefit of ART in HIV type-1 infection has been attributed primarily to its suppression of viral replication as demonstrated in clinical trials [14-15]. Recent observations suggest that HIV may be more susceptible to combination therapy during acute infection [16-17]. Early in the course of infection, the immune system remains relatively intact, although the rate of loss of CD4+ cells may be increasing as acute HIV infection progresses [18-19]. Several observational studies have reported that even those patients who have virological failure may have a sustained positive CD4+ cell count response [15, 20]. In a report from Swiss COHORT, interruption of ART was associated with a significant decrease in CD4+ cells suggesting that adherence to ART, not viremia, is the most significant factor in predicting CD4+ cell count [15].

CONCLUSION:

Results of the present study suggest that CD4+ cell counts of HIV patients does not correlate with inclusion of non-nucleoside reverse transcriptase inhibitor, Efavirenz or Nevirapine in treatment regime and it need to study in detail to find out the factors playing role in it.

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REFERENCES

1. Anthony SF and Lane HC. Human Immunodeficiency Virus (HIV) disease: AIDS and related disorders. In : Eugene Braunwald, Anthony S. Fauci, Dennis L. Kasper, Stephen L. Hauser, Dan L. Longo, J. Larry Jameson. (Editors). Harrison's principles of Internal Medicine. 15th edition. McGraw-Hill, New York; 2001. p 1878.
2. Lang N, Parkins H, Andersen RE, Royce R, Jewell N. Pattern of T lymphocyte changes with human immunodeficiency virus infection from seroconversion to the development of AIDS. J AIDS. 1989; 2: 63-69. PMid:2783971
3. The opportunistic infections project team of the collaboration of observational HIV epidemiological research in Europe (COHERE) in EuroCoord. CD4 cell count and the risk of AIDS or death in HIV-infected adults on combination antiretroviral therapy with a suppressed viral load: A longitudinal cohort study from COHERE. PLoS Med. 2012; 9(3): e1001194. http://dx.doi.org/10.1371/journal.pmed.1001194 PMid:22448150 PMCid:PMC3308938
4. Hugh MD, Stein DS, Gundacker HM, Valentine FT, Phair JP. Within subset variation in CD4 lymphocyte count in asymptomatic human immunodeficiency virus infection – implications for patient monitoring. J Infect Dis. 1994; 169: 28-36. http://dx.doi.org/10.1093/infdis/169.1.28
5. Sabin Caroline. Response to combination antiretroviral therapy: variation by age. AIDS. 2008; 22:1463–1473. http://dx.doi.org/10.1097/QAD.0b013e3282f88d02 PMid:18614870
6. Centres for Disease Control and Prevention. Guidelines for the performance of CD4+ T cells determination in persons with human immunodeficiency virus infection. Morbid Mortal Wkly Rep. 1992; 44 (RR-8): 1-17.
7. National Institute of Health. Recommendation for zidovudine-early infection. JAMA. 1990; 263: 1606-1609. http://dx.doi.org/10.1001/jama.263.12.1606 http://dx.doi.org/10.1001/jama.1990.03440120014002
8. Centre for Disease Control. Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. Morbid Mortal Wkly Rep. 1992; 41 (RR-17): 1-19.
9. Kannangai R, Ramalingam S, Vijaykumar TS. The immunological and virological response in human immunodeficiency virus type-1 (HIV-1) infected Indian individuals on HAART therapy: a one-year follow up study. Indian J Med Microbiol. 2003; 21(4): 274-276. PMid:17643043
10. Olsen CH, Mocroft A, Kirk O, Vella S, Blaxhult A. Interruption of combination antiretroviral therapy and risk of clinical disease progression to AIDS or death. HIV Medicine. 2007; 8: 96–104. http://dx.doi.org/10.1111/j.1468-1293.2007.00436.x PMid:17352766
11. WHO Scaling up antiretroviral therapy in resource-limited settings – 2003 Revision: p 24.
12. Opravil M, Lederberger B, Hansjakob F. Clinical efficacy of early initiation of HAART in patients with asymptomatic HIV infection and CD4 cell count >350x106/L. AIDS. 2002; 16(10) :1371-1381. http://dx.doi.org/10.1097/00002030-200207050-00009 PMid:12131214
13. Rebachandra H, Brajachand Ng, Rakshit P, Priya E. Enumeration of CD4+ and CD8+ T lymphocytes in healthy HIV seronegative adults of north-east India – a preliminary study. J of Med Society. 2006; 20(1): 2-6.
14. DeHovitz JA, Kovacs A, Feldman JG. The relationship between virus load response to highly active antiretroviral therapy and change in CD4 cell counts: a report from the women's interagency HIV study. J Infect Dis. 2000; 182: 1527-1530. http://dx.doi.org/10.1086/315875 PMid:11010840
15. Mocroft A, Phillips AN, Gatell J, Ledergerber B, Fisher M. Normalisation of CD4 counts in patients with HIV-1 infection and maximum virological suppression who are taking combination antiretroviral therapy: an observational COHORT study. Lancet. 2007; 370: 407–13 http://dx.doi.org/10.1016/S0140-6736(07)60948-9
16. Hammer SM, Squires KE, Hughes MD. A controlled trial of two nucleoside analogues plus Indinavir in persons with human immunodeficiency virus infection and CD4 cell counts of 200 per cubic millimeter or less. N Engl J Med. 1997; 337: 725-733. http://dx.doi.org/10.1056/NEJM199709113371101 PMid:9287227
17. Hogg RS, Yip B, Chan KJ. Rates of disease progression by baseline CD4 cell count and viral load after initiating Triple-Drug therapy. JAMA. 2001; 286: 2568-2577. http://dx.doi.org/10.1001/jama.286.20.2568 PMid:11722271
18. Sinicco A, Fora R, Raiteria R. Is the clinical course of HIV-1 changing? Cohort study. BMJ. 1997; 314: 1232-1237. http://dx.doi.org/10.1136/bmj.314.7089.1232 PMid:9154026 PMCid:PMC2126619
19. Rosenberg Es, Altfeld M, Poon Sh. Immune control of HIV-1 after early treatment of acute infection. Nature. 2000; 407: 523-526. http://dx.doi.org/10.1038/35035103 PMid:11029005
20. Lucas GM, Caisson Re, Moore RD. Highly active antiretroviral therapy in large urban clinic: risk factors for virologic failure, and adverse drug reactions. Ann Intern Med. 1999; 131: 81-87. http://dx.doi.org/10.7326/0003-4819-131-2-199907200-00002 PMid:10419445