

## ORIGINAL ARTICLE

Title; Efficacy of antiviral treatment on HIV<sup>+</sup> patients and CD4<sup>+</sup> TcellSeyyed Abbas Hashemi<sup>1</sup> Saeid Abediankenari<sup>2</sup> Farhang Babamahmoodi<sup>3</sup> Mohammad Reza Parsai<sup>4</sup>

Received: 15 september 2012 / Accepted: 16 october 2012

**Abstract**

**Background:** Acquired immunodeficiency syndrome is an important infectious disease in contamination of committed T cells. There is a global widespread infection of HIV. The end stage of HIV infection is one of the most causes of death across the world. HIV transmission can be introduced by infecting CD4<sup>+</sup> cells.

**Objective:** For understanding the progression of virus and usefulness of treatment, we measured the number of CD4<sup>+</sup> cells change.

**Materials and Methods:** We monitored the count of CD4<sup>+</sup> cells by Flowcytometry before and during treatment of HIV infected people by Ziduvudine 100 mg twice a day, Lamivudine 150 mg twice a day and Nevirapin 200 mg a day, retrospectively.

**Results:** The study population included 195 HIV positive patients, 87.1% men and 12.8% women. Most of infected patients were older than 40 years old (29.2%). CD4 counts of 20 patients were less than 350 and received treatment. Patients with CD4 count

less than 350 withdrew antiviral therapy. At first stage of treatment, patients with CD4 count less than 100 were 58.3% of infected patients but after treatment with antiviral drugs for six months it decreased to 33%. CD4 count of 25% of these people changed to more than 350 while before cure we did not have CD4 count more than 350 among these patients.

**Conclusion:** After six months treatment, 25% of patients CD4 count reached to more than 350 and showed that at early stage of AIDS we can control the disease and therapy can have beneficial effects in some patients.

**Key words:** HIV, Ziduvudine, Lamivudine, Nevirapin, CD4 count

1-Faculty Of Medicine, Student Research Committee, Mazandaran University Of Medical Sciences, Sari IRAN

2-Microbiology And Immunology Department, Faculty Of Medicine, Mazandaran University Of Medical Sciences, Sari IRAN

3-Department Of Infectious And Tropical Disease, Faculty Of Medicine, Mazandaran University Of Medical Sciences, Sari IRAN

4-Health Center Of Mazandaran Province, Sari, Iran

Corresponding Author: Dr Saeid Abediankenari (PhD)

Email: abedianlab@yahoo.co.uk; abbas.hashemi30@gmail.com

Fax: 00981513543248

Po.Box: 48175-1665

## Introduction

For the last decades, there has been a universal spread of human immunodeficiency virus (HIV). The result of HIV infection is one of the most reason of death across the world. Acquired immunodeficiency syndrome (AIDS) progression is different among infected patients. Studies showed that some patients resistant to virus which depends on type of virus and host features. Different methods are existing for treatment and prevention(1-4). Self-administering prophylactic materials such as microbiocides limit the transmission of HIV and sexual transmitted diseases. HIV transmission can be defined by virus crossing the epithelial surface and infecting CD4<sup>+</sup> cells. The entry of HIV into CD4<sup>+</sup> cells is mediated by different glycoproteins which exist on the viral envelope(5-13). So the number of CD4<sup>+</sup> cells during treatment will be affected by drugs and virus but it is unclear. To find out the progression of HIV and utility of therapy, the number of CD4<sup>+</sup> cells change is necessary. The purpose of this study was evaluation of HIV positive patients' condition before and after treatment of HIV infection by antiviral drugs.

## Method and Material

### -Ethical Approval

This study was approved by the Ethics Committee of the Mazandaran University of Medical Sciences, Sari, IRAN.

### -Patients and Samples

In this retrospective study ,we examined patients with HIV newly diagnosed who

were referred to infectious diseases researches center in sari Tooba clinic and ghemshar Razi hospital (Mazandaran province of IRAN ) for diagnosis and treatment. Patients with CD4<sup>+</sup> count less than 350 had been considered for receiving antiviral treatment with Ziduvudine 100 mg twice a day, Lamivudine 150 mg twice a day and Nevirapin 200 mg a day. We took 5 ml of peripheral whole blood of the patients. Then, we isolated peripheral blood mononuclear cells with Ficoll histopaque 1.077(sigma, USA).

### -Flow cytometry

Mononuclear cells were stained with FITC-anti-CD4 or isotype control antibodies (DAKO, Germany) for 30 min at 4°C. Surface expressions of the antigens were measured by Flowcytometry (patec pas, Germany).

### -Statistical Analysis

The procedures included were transcription, preliminary data inspection, content analysis and finally interpretation. Statistical analysis was performed with SPSS software (version 16, Chicago, IL, USA).

## Results

The study population included 195 HIV positive patients that 87.1% (170 patients) of those were men and 12.8% (25 patients) women. 29.2% of infected patients were older than 40 years old (Table 1). Twenty patients with CD4 count less than 350/μl needed to receive drugs but 12 patients were

screened and other 8 patients ruled out since they did not return to center for treatment. The features of these twenty patients have been showed at table 2. At the beginning of treatment of these twenty patients, individuals with CD4 count less than 100 were 58.3% (7 patients) of study population but after six months treatment with antiviral

prescriptions, it switched to 33%(4 patients). For patients whom CD4 count was among 100-200, the count was 16.6% (2 patients) and improved to 25% (3 patients). At the onset, there were no patients with CD4 count more than 350, whereas after these regimens, CD4 count of 25% (3 patients) changed to more than 350 (Table3).

Table 1.Characteristic of study population in the Mazandaran province of Iran

<b>Gender</b>	<b>Female</b>	<b>25(12.8%)</b>
	<b>Male</b>	<b>170(87.1%)</b>
<b>Age (years)</b>	<b>≤25</b>	<b>2(1%)</b>
	<b>25-30</b>	<b>11(5.6%)</b>
	<b>31-35</b>	<b>30(15.3%)</b>
	<b>36-40</b>	<b>32(16.4%)</b>
	<b>&gt;40</b>	<b>57(29.2%)</b>
	<b>Missing</b>	<b>63(32.3%)</b>
<b>Marital States</b>	<b>Currently Married</b>	<b>57(29.2%)</b>
	<b>Got divorced</b>	<b>22(11.2%)</b>
	<b>Single</b>	<b>31(15.8%)</b>
	<b>Missing</b>	<b>85(43.5%)</b>

Table 2.Characteristic of patients with CD4 Count less than 350

<b>Addiction</b>	<b>Not addicted</b>	<b>9(45%)</b>
	<b>Addicted</b>	<b>11(55%)</b>
<b>Among the addicted patients</b>	<b>IV drug abuser</b>	<b>3(15%)</b>
	<b>Methadone</b>	<b>4(20%)</b>
<b>Respiratory tract infection</b>	<b>Pneumonia</b>	<b>9(45%)</b>
	<b>TB</b>	<b>2(10%)</b>

Table 3. Number of CD4 Count before and after six months administration of Ziduvudine, Lamivudine and Nevirapin in patients with CD4 Count less than 350

<b>CD4 Count before treatment</b>	<b>&gt;350 cell/μl</b>	<b>0(0%)</b>
	<b>201-350 cell/ μl</b>	<b>3(25%)</b>
	<b>100-200 cell/ μl</b>	<b>2(16.6%)</b>
	<b>&lt;100 cell/ μl</b>	<b>7(58.3%)</b>
<b>CD4 Count after treatment</b>	<b>&gt;350 cell/ μl</b>	<b>3(25%)</b>
	<b>201-350 cell/ μl</b>	<b>2(16.6%)</b>
	<b>100-200 cell/ μl</b>	<b>3(25%)</b>
	<b>&lt;100 cell/ μl</b>	<b>4(33.3%)</b>

### Discussion

In this study, we compared the percentage of CD4<sup>+</sup> cells in HIV positive patients before and during treatment to elucidate antiretroviral regimens efficacy in progression of disease. The patients with low CD4<sup>+</sup> cells are high risk for peripheral neuropathy, lactic acidosis and lipoatrophy and other metabolic complications (14-20). TB is an important world health concerning problem that will affect the industrialized nations more. The main cause is aside from TB/HIV co-infection, is the increase of resistant TB strains. The condition is serious since of the spread of multidrug-resistant TB (21). In this study, we observed 55% of the patients had respiratory disorders including 10% TB infection and 45% pneumonia.

At the present study, patients with CD4 count less than 350 underwent antiviral

therapy with Ziduvudine 100 mg twice a day, Lamivudine 150 mg twice a day and Nevirapin 200 mg a day. Our findings revealed that among the patients who got therapy for six months, CD4 count of 3 patients (25%) changed to more than 350. Although our results were significantly different before and after treatment, but the question is why we cannot control all patients and cure them forever. In spite of this therapy, after several months, CD4 count of some patients came down and they died. Primary outcomes were useful but we showed that some patients had drug resistance. So, in future, we may need to change the drugs doses. There were several limitations which not resolved by this study, although these regimens seemed to be beneficial but we did not monitor other drugs effect such as co-trimoxazole to

realize that they have positive or negative effect on immune system. Moreover, we can't eliminate these drugs because they inhibit other infections in these patients and if we exclude them it seems to get converse effect. So, further investigations may be required to be done to classify different drugs doses at various stages of disease on more patients.

### Acknowledgment

This study has been supported by Mazandaran University of medical science. The authors are grateful to Sarvenaz Azarnoosh for technical assistance.

### Reference

1. Carrington M, Nelson G, O'Brien SJ. Considering genetic profiles in functional studies of immune responsiveness to HIV-1. *Immunology Letter* 2001; 79: 131-140.
2. Michael NL, Host genetic influences on HIV-1 pathogenesis. *Curr Opin Immunol* 1999; 11: 466-474.
3. Kumar V, Prakash O, Manpreet S, Sumedh G, and Medhi B. Genetic basis of HIV-1 resistance and susceptibility: an approach to understand correlation between human genes and HIV-1 infection. *Indian J Exp Biol* 2006; 44: 683-692.
4. Kaur G and Mehra N. Genetic determinants of HIV-1 infection and progression to AIDS: susceptibility to HIV infection. *Tissue Antigens* 2009; 73: 289-301
5. Reeves JD, McKnight A, Potempa S, Simmons G, Gray PW, Power CA and et al. CD4 independent infection by HIV-2 (ROD/B): use of the 7-transmembrane receptors CXCR-4, CCR-3, and V28 for entry. *Virology* 1997; 231: 130-134.
6. Rucker J, Edinger AL, Sharron M, Samson M, Lee B, Berson JF, et al. Utilization of chemokine receptors, orphan receptors and herpes virus-encoded receptors by diverse human and simian immunodeficiency viruses. *J Virology* 1997; 71: 8999-9007.
7. Combadiere C, Salzwedel K, Smith ED, Tiffany HL, Berger EA and Murphy PM. Identification of CX3CR1. A chemotactic receptor for the human CX3C chemokine fractalkine and a fusion coreceptor for HIV-1. *J Biol Chem* 1998; 273: 23799-23804.
8. Alkhatib G, Combadiere C, Broder CC, Feng Y, Kennedy PE, Murphy PM and Berger E. A CCR5: a RANTES, MIP-1alpha, MIP-1beta receptor as a fusion cofactor for macrophage-tropic HIV-1. *Science* 1996; 272: 1955-1958.
9. Choe H, Farzan M, Sun Y, Sullivan N, Rollins B, Ponath PD and et al. The beta-chemokine receptors CCR3 and CCR5 facilitate infection by primary HIV-1 isolates. *Cell* 1996; 85: 1135-1148.
10. Deng H, Liu R, Ellmeier W, Choe S, Unutmaz D, Burkhart M and et al. Identification of a major co-receptor for primary isolates of HIV-1. *Nature* 1996; 381: 661-666.
11. Doranz BJ, Rucker J, Yi Y, Smyth RJ, Samson M, Peiper SC, et al. A dual-tropic primary HIV-1 isolate that uses fusin and the beta-chemokine receptors CKR-5, CKR-3, and CKR-2b as fusion cofactors. *Cell* 1996; 85: 1149-1158.

12. Dragic T, Litwin V, Allaway GP, Martin SR, Huang Y, Nagashima KA, *et al.* HIV-1 entry into CD4+ cells is mediated by the chemokine receptor CC-CKR-5. *Nature* 1996;381: 667–673
13. Cohen OJ, Paolucci S, Bende SM, Daucher M, Moriuchi H, Moriuchi M, *et al.* CXCR4 and CCR5 genetic polymorphisms in long-term non progressive human immunodeficiency virus infection: lack of association with mutations other than CCR5-Delta32. *J Virology* 1998; 72: 6215–6217
14. Scarsella A, Coodley G, Shalit P, Anderson R, Fisher RL, *et al.* Stavudine-associated peripheral neuropathy in zidovudine-naïve patients: effect of stavudine exposure and antiretroviral experience. *Adv Therapy* 2002; 19: 1–8.
15. Reliquet V, Mussini JM, Chenebault JM, Lefeuvre A, Raffi F .Peripheral neuropathy during stavudine-didanosine antiretroviral therapy. *HIV Med* 2001; 2: 92–96.
16. Miller KD, Cameron M, Wood LV, Dalakas MC, Kovacs JA .Lactic acidosis and hepatic steatosis associated with use of stavudine: report of four cases. *Ann Intern Med* 2000; 133: 192–196.
17. Mokrzycki MH, Harris C, May H, Laut J, Palmisano J .Lactic acidosis associated with stavudine administration: a report of five cases. *Clin Infect Disease* 2000;30: 198–200.
18. Joly V, Flandre P, Meiffredy V, Leturque N, Harel M, *et al.* Increased risk of lipoatrophy under stavudine in HIV-1-infected patients: results of a substudy from a comparative trial. *AIDS* 2002; 16: 2447–2454.
19. van Griensven J, De Naeyer L, Mushi T, Ubarijoro S, Gashumba D, *et al.* High prevalence of lipoatrophy among patients on stavudine-containing first-line antiretroviral therapy regimens in Rwanda. *Trans R Soc Trop Med Hyg* 2007; 101: 793–798.
20. Nachega JB, Trotta MP, Nelson M, Ammassari A .Impact of metabolic complications on antiretroviral treatment adherence: clinical and public health implications. *Curr HIV/AIDS Rep* 2009; 6: 121–129.
21. Loddenkemper R, Hauer B. Drug-resistant tuberculosis: a worldwide epidemic poses a new challenge. *Dtsch Arztebl Int.* 2010 Jan;107(1-2):10-9. Epub 2010 Jan 7.