Original Article

HIV AIDS

Response of Antiretroviral Therapy (Ziduvidune, Lamivudine, Niverapine) in Patients Suffering from Acquired Immuno Deficiency Syndrome (AIDS)

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ABSTRACT

Objective: Purpose of current study was to evaluate the effect of antiretroviral drugs (Three regimen) Ziduvodine, Lamivudine and Niverapine to HIV patients presented in D.G. Khan Zone in regard to CD4 level and viral loads before start of drugs and after one year treatment.

Study Design: Comparative study

Place and Duration of Study: This study was carried out at the Institute of Molecular Biology and Biotechnology, and Centre for Research in Molecular Medicine, The University of Lahore-Pakistan from April 2013 to June 2014.

Materials and methods: Seventy five (75) patients suffering from HIV and thirteen (13) control individuals were selected for the study. Rapid testing and ELISA screening were performed for identification of presence/absence of virus and antibodies respectively. Viral load and CD4+ absolute count were also evaluated by PCR and Multiset software respectively. All the analytical work was performed at the Institute of molecular biology and biotechnology (IMBB), and Centre for research in molecular medicine (CRiMM), The University of Lahore-Pakistan.

Results: Statistically highly significant difference (P=.000) was observed regarding viral load before and after the treatment in HIV patients receiving combination therapy, ART (antiretroviral therapy). The viral load in control and HIV patients before and after the treatment was (0.00, $3.23x10^4$) and (0.00, $1.45x10^2$) respectively. Levels of CD4+ cells were increased and a highly significant difference was recorded among control and ART treated patients. Inverse correlation was recorded between viral loads (After) and CD4+ levels (After), (Viral Load Vs CD4+, r = -.678**).

Conclusion: It can be concluded that ART is highly effective in AIDS patients with minimal adverse effects, makes the life of AIDS patients less miserable and improve the quality of life.

Key Words: Antiretroviral drugs, ART, Ziduvodine, Lamivudine, Niverapine, ELISA, CD4+, PCR, viral load, HIV AIDS.

INTRODUCTION

Human Immuno deficiency virus was discovered in 1983. Initially it was mainly found in the people who were involved in homo sexuality also named as Gay cancer. It is believed that this virus is transmitted from animals to human beings. It is believed that it is a virus generated in labs to be used in biological weapons but eventually escaped and later entered in the genome of animals from where it is transmitted to human beings (WHO, 2009)[1]. On the clinical manifestations, the disease was named as Acquired immunodeficiency Syndrome with acronym of AIDS. ART is recommended for all people infected with HIV. ART involves taking a combination of anti-HIV medication (a regimen). Everyday ART is a lifelong treatment (Zhou et al., 2010)[2]. The detection of a virus from the lymphocytes of the AIDS patients was done in 1984 independently by Robert Gallo at the National Institute of Health, USA and Montagnier at the Pasteur Institute, Pairs.

According to the WHO committee on AIDS in (2009)[1] stated, that prevention of HIV infection should be the most seeking task as disease was spreading very rapidly. A joint venture for awareness, pre-cautions, prevention & treatment should be initiated and managed accordingly with different stake holders like Government Institutions NGOs, Pharmaceutical Industry and research institution. Nucleoside reverse transcriptase inhibitors (NRTIs), Non nucleoside reverse transcriptase inhibitors, (NNRTIs), protein inhibitors and some other drugs are also available that inhibit viral process to make copies of itself.

MATERIALS AND METHODS

Inclusion criteria for studies: Patients form both genders, ages groups include children up to 60 years of age. The study was conducted from April 2013 to June

2014. Seventy five (75) patients suffering from HIV and thirteen (13) control individuals were selected for the study from Dera Ghazi Khan. All the analytical work was performed at the Institute of molecular biology and biotechnology (IMBB), and Centre for research in molecular medicine (CRiMM), The University of Lahore-Pakistan.

Following criteria was adopted to start anti-retro viral therapy.

1. Patient was a confirmed case of HIV/AIDS by rapid testing, by ELISA screening of detection of anti bodies and viral load by PCR.
2. CD4 absolute count. CD4 absolute count should be less than 350 cells/micro ml (normal range 450-1100)
3. Clinical Staging of the patients was determined.
4. Incidence of repeated opportunistic infection along with repeated Diarrhea.

Exclusion criteria:

1. Age above 70 years
2. CD4 absolute count more than 350 cells/micro ml.
3. Patient not willing to start antiretroviral therapy.

Methodology:

Rapid testing: 3CC of venous blood was taken and centrifuged, serum was separated and put on rapid kit along with buffer if 2 lines are appearing patient was positive. In case of negative only control line appeared on device. The first line was for control and second line was for patient (test).

ELISA Screening: Antibodies were detected by sandwich method of labeled prefilled antigen-antibody mixture and were compared with cut off ratio and determined the reactivity.

Viral Load by PCR: PCR facility was provided by Centre for Research in Molecular Medicine (CRiMM) and Institute of Molecular Biology and Biotechnology (IMBB), the University of Lahore, Lahore.

CD4 absolute Count: The absolute CD4 & CD8 count (absolute number of positive cellular events in sample compared to beads events) was determined by Multiset software and expressed in cells/ µl.

RESULTS

Data presented in Table-1 shows statistically highly significant difference (P=.000) was observed regarding viral load before and after the treatment in HIV patients receiving combination therapy, ART (Ziduvidune-Lamivudine-Niverapine). The viral load in control and HIV patients before and after the treatment was (0.00, $3.23x10^4$) and (0.00, $1.45x10^2$) respectively. The data regarding CD4+ cells depicted in table 01 also shows that with combination therapy, ART (Ziduvidune-Lamivudine-Niverapine), the levels of CD4+ cells was increased and a highly significant difference was recorded among control and ART treated patients. The CD4+ cells levels in control and HIV patients before and after the treatment was (340.38, 196.77) and (188.59, 388.33) respectively. Data in table 03 (Pearson Correlation, Two Tailed**)** shows that a highly significant inverse relationship between viral load (Before) and CD4+ cell levels (Before) (Viral Load Vs CD4+, r = -.633**). Likewise inverse correlation was also recorded between viral loads (After) and CD4+ levels (After), (Viral Load Vs CD4+, r = -.678**).

Table No.1: Comparison of viral load and CD4+ among control and patients

	Group	n	Mean±SD	P value
Viral load (before)	Control	13	0.00±0.00	.000
	Patient	75	$3.23x10^4$±0.67	
Viral load (after)	Control	13	0.00±0.00	.000
	Patient	75	$1.45x10^2$±0.24	
CD4+ (before)	Control	13	340.38±81.35	.000
	Patient	75	188.59±23.59	
CD4+ (after)	Control	13	196.77±54.24	.000
	Patient	75	388.33±34.42	

Viral load: copies/mm CD4+: cells/mm^3

Table No.2: Pearson Correlation

	Viral load (before)	Viral load (after)	CD4+ (before)	CD4+ (after)
Viral load (before)	1	-.560**	-.633**	.569**
		.000	.000	.000
Viral load (after)		1	.827**	-.678**
			.000	.000
CD4+ (before)			1	-.685**
				.000
CD4+ (after)				1

**. Correlation is significant at 0.01 level (2-tailed)

DISCUSSION

Bartlett et al., (2002)[3] reported that combination of two nucleoside reverse transcriptase inhibitor suppress HIV much better as compared with single NRTI. Popular nucleoside reverse transcriptase inhibitors in combination are tenovofir along with emtricitabline in resource rich regions. These two drugs are co formulated as a single drug and are advised once a day. Abacavir with lumividine is other combination but abacavir need sensitivity testing before administration. Mehandru (2004)[4] reported that combination antiretroviral therapy has a beneficial effect on laboratory markers of disease progression. Early treatment could decrease severity of acute disease; alter earlier viral set point, reduce rate of viral mutation, suppression of viral replication increase in immune function and reduce risk of viral transmission during high infectious stage of disease.

Zhou et al., (2010)[2] concluded that combination antiretroviral treatment increased CD4 level and decreased viral load in HIV1 Patient. They also stated that in order to get positive CD4 slope treatment need to start at early stage of disease. Auvert et al., (2005)[5] reported that antiretroviral therapy reduced HIV viral load in seminal fluid and cericovaginal secretions. They concluded that use of Zidovudine in HIV infected men decreased 50% risk of HIV transmission in their female sexual partners. Attia et al., (2009)[6] observed that there is no transmission of HIV in heterosexual patient with viral load below 400copies/ml and receiving antiretroviral therapy. They concluded that transmission can be reduced by 92% from 5.64 to 0.46 per 100 persons in patient on ART and non ART. Melbourne et al., (1999)[7] reported that best results against HIV can be achieved when patient take total prescribed antiretroviral doses at appropriate time. Those patients that take almost 90% doses but not at correct time, could not achieve successful treatment rate. The dose fluctuation was seen in 50% patients in early two months of treatment. The dose fluctuation was among those patients that took medicine within two hours of prescribed dose time and after two hours.

Kastrissios et al., (1998)[8] concluded that consequences of missed doses results in increasing viral load and development of mutant strains. As drug level fall below critical point, HAART inhibitory effect on viral replication may lessen, resulting in increased viral replication and viral load. Ariyoshi et al., (2000)[9] stated that HIV-2 infections are associated with lower plasma viral load and slower decline in CD4 count as compared to HIV-1 infections. However in short follow up treatment cases disease progress to advance stage. Mocroft et al., (2006)[10] concluded that CD4 level decreased significantly in HIV patients with viral load greater than 10,000copies/ml regardless of CART regimen used. Moreover response of CART was much better than of CART and NRTIS were better than NNRTIs. Single antiretroviral drug combination of two or more antiretroviral drug can suppress the HIV much better. They stated that combination ART achieves lifelong suppression of HIV replication but treatment is needed to continue for long duration. High cost of treatment in resource poor region limit the treatment rate and also control of HIV does not fully restore health in patient. Schapiro et al., (1999)[11] concluded that there are significant mutational drift in HIV and different patients are infected with different genotypes of HIV virus. Antiretroviral drug may eliminate the viral load but if resistance strains are present, they rapidly replace the eliminated viruses (Martinez et al., 2003)[12]. So it is better to advice combination antiretroviral therapy of three or four drugs from two different classes.

CONCLUSION

It can be concluded that ART is highly effective in AIDS patients with minimal adverse effects, makes the life of AIDS patients less miserable and improve the quality of life.

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