Research Paper   **Medical Science**

To Study of The Effects of Triple Anti-Retroviral Therapy On Cd4 Count and To Compare With The Clinical Efficacy and Laboratory Monitoring.

Dr Aher Sangeeta	MD (G.Medicine)
Dr Phulpagar Mayura	MD (Pathology)
Dr Chaugule Hemant	MD

ABSTRACT

• Human immunodeficiency virus (HIV) positive patients continue to have raise in CD4 cell for several years after initiation of anti-retroviral therapy1,10,13 .In developing countries the standard methods used to monitor HIV disease progression and therapy response are clinical assessment, CD4+ T lymphocyte count measurement, and plasma viral load (PVL) quantification4. The aims and objectives of this study was to compare the clinical efficacy of triple antiretroviral regimens in adults who tested positive for antibodies to HIV-13.(1).To see effect of three ART regime on CD4 count at baseline and after six month of ART.(2).To correlate CD4 count changes with type of ART regime. (3)To analyze side effects after six month of ART.Methodology: This is a continuous, longitudinal, prospective follow up study of 159 patients conducted in a single ART Centre of Mumbai We performed indirect comparisons between these triple regimens .Materials and methods A total 159 of HIV-1 infected patients newly detected and treatment naive patients attending ART Centre in a tertiary Hospital Mumbai were recruited for the study. All these patients were evaluated for their CD4 Count by using BD Flowcytomter and their plasma RNA Viral Load by Taqman Probes using Roche RT-PCR machine.

Result :1] Out of 159, 92 patients were male and 67 were female. Most patients were in age group 31 to 40 years (40.88%).2]Distribution of study group as per ART Regime were ZLN-37.74%, SLN-33.96%, ZLE-28.30%. 3] Distribution of anemia as per ART regime-11.7% developed anemia in ZLN group, 7.4% developed anemia in SLN group and 2.2% developed anemia in ZLE group ,7,8 4] Association among study group as per Transaminitis was ZLN-13.3%, SLN-7.4%, ZLE-0%.Transaminitis was seen in patients on Nevirapine based regime. 5] There was no correlation between dyslipidemia in any particular ART regime ZLN-37.74%, SLN-33.96%, ZLE-28.30%. Distribution of study group as per Dyslipidemia was ZLN-8.3%, SLN-7.4%, ZLE-2.2%. (6)Baseline CD4 count was in ZLN-246.6%, SLN-251.3%, ZLE-253.3%. (7)Comparison among study group for cd4 count at 6 month was ZLN-314.65%, SLN-300.54%, ZLE-282.36%. Maximum average increase in CD4 count after 6 month of ART was seen in ZLN group however most adverse effects were seen in ZLN group like skin rashes (7.25%), anemia (6.5%) and nausea/vomiting (5.5%) were common .

KEYWORDS   CD4+ T lymphocyte count (CD4 count); HIV; highly active antiretroviral therapy (HAART).

1.Introduction As per National AIDS Control Organization (NACO) Guidelines HIV-1 infected patients are treated with either one of the primary line regimen as follows SLN (Stavudine + Lamivudine + Nevirapine) ZLN (Zido-vudine + Lamivudine + Nevirapine), SLE (Stavudine + Lamivudine + Efavirenz), ZLE (Zidovudine + Lamivudine + Efavirenz)[11,12,14].Many different combinations of highly active antiretroviral therapy regimens are available[5]. Triple antiretroviral therapy is superior to dual therapy for preventing progression to AIDS or death in patients with advanced disease.The aims and objectives o**f** this study was to compare the clinical efficacy of triple antiretroviral regimens in adults who tested positive for antibodies to HIV-1[3].

- To see effect of three ART regime on CD4 count at baseline and after six month of ART.
- To correlate CD4 count changes with type of ART regime.
- To analyze side effects after six month of ART.

2. Materials and methods
2.1 Sample size: 159 new HIV positive patients who satisfied inclusion and exclusion criteria and gave written consent were included in study that was carried out in a tertiary care hospital during the period of two years (2010 to 2012).

Inclusion criteria:
[1.] HIV positive by ELISA. [2.] Patients stared on ART by ART Centre as per NACO/ WHO guidelines. [3.]Baseline CD4 counts between 200 to 300 [4.]Willingness to give written informed consent

Exclusion criteria: 1].Pregnant and lactating female.2.Opportunistic infection except T.B.

Study design: It was prospective observational cohort study conducted in tertiary care hospital.Indoor and OPD.Patient total no 159 ,who were HIV positive were included in the study after Ethics committee clearance .Subjects were divided into three study groups depending on ART regime as follow

Regime 1- T. Zidovudine 300mg bd , T. Lamivudine 150mg bd and T. Nevirapine 200mg bd .[ZLN]

Regime 2- T.Stavudine 30mg bd , T. Lamivudine 159mg bd and T. Nevirapine 200mg bd.[SLN]

Regime 3- T. Zidovudine 300mg bd ,T. Lamivudine 150mg bd and T. Efavirenz 600mg od .[ZLE]

2.3 Experimental methods: Subjects clinical profile , routine investigation , lipid profile and CD4 counts were analyzed before starting ART and after 6 month of ART.

2.4 Statistical analysis: Kruskal-Wallis One Way Analysis of

Variance on Ranks test ,Oneway ANOVA test . Chi-Square Study, Pearson Chi-Square applied,

3.Result :1] Out of 159, 92 patients were male and 67 were female. Most patients were in age group 31 to 40 years (40.88%). The sex difference was not statistically significant. **Table No 1**

2]Distribution of study group as per ART Regime were ZLN-37.74%, SLN-33.96%, ZLE-28.30%. **3]** Distribution of anemia as per ART regime-11.7% developed anemia in ZLN group, 7.4% developed anemia in SLN group and 2.2% developed anemia in ZLE group. Chi-Square Study Value 3.289 df 2 P value 0.193 Association is Not significant. There was no correlation between anemia and any particular ART regime. ZLN-11.7%SLN 7.4% -ZLE-2.2%.4] Association among study group as per Transaminitis was ZLN-13.3%, SLN-7.4%, ZLE-0%**.**Transaminitis was seen in patients on Nevirapine based regime**.** 5] There was no correlation between dyslipidemia in any particular ART regime ZLN-37.74%, SLN-33.96%, ZLE-28.30%. Distribution of study group as per Dyslipidemia was ZLN-8.3%, SLN-7.4%, ZLE-2.2%. Chi-Square Study Value 1.803 df 2, P value 0.406 Association is Not significant. 6] Distribution of study group as per Skin rash -6.92% .Patients developed skin rash.ZLN-5%, SLN-14.8%, ZLE-0 %. Chi-Square Study Value 8.916 df 2 P value 0.012 Association is significant . 6)Baseline CD4 count was in ZLN-246.6%, SLN-251.3%, ZLE-253.3%. **Table No 2.** (7)Comparison among study group for cd4 count at 6 month was ZLN-314.65%, SLN-300.54%, ZLE-282.36%. **Table No 3.**Most adverse effects were seen in ZLN group. **Table 4.**

DISCUSSION: In this study 159 HIV positive cases on ART of a tertiary care hospital were taken. Patients' CBC, RFT, LFT, Lipid profile, RBS and CD4 count were analyzed   before and after 6 month of ART.　　　　Out of 159, 92 (57.8%) were male and 67 (42.20%) were female. Mean age group 40.88% years. The age and sex difference was not statistically significant in the three groups.　 Baseline average CD4 count was 246.62 in ZLN group, 251.28 in SLN group and 253.27 in ZLE group. The difference of baseline average CD4 count was not statistically significant in the three groups[2]. Average increase in CD4 count after 6 month of ART was 68.03 in ZLN group; 49.26 in SLN group and 29.09 in ZLE group. The difference of average increase in CD4 count after 6 month of ART was statistically significant in the three groups[5]. In our study 12 (7.55%) out of 159 patients developed anemia. This difference was not statistically significant Max and Sherer (2000) [9]write that it can be observed in 1 to 7 % of Zidovudine users. Ajay Sharma, et al (2007) [14] in a study found the incidence of anemia to be 43% .Elevation of liver enzymes was observed in 12(7.55%) patients, all were on Nevirapine based regime, this difference was statistically significant[6].Dyslipidemia was found in 10 (6.29%) in our study, 5 (3.14%) developed dyslipidemia in ZLN group, 4 (2.52%) developed in SLN group and 1 (0.06%) developed in ZLE. This difference was not statistically significant. Skin rash was observed in 11(6.92%) in our study, 3 (1.89%) developed skin rash in ZLN group, 8 (5.03%) developed skin rash in SLN group. Skin rash was seen in patients taking NVP based regimens. Our study goes in agreement with Max and Sherer (2000) [9]and is very much comparable to findings of Sharma et al (2008)[11]reported that 26% of females and 22% of males on NVP developed rash. This difference was statistically significant[6.] 7 patients on ZLN regimen, had viral load more than 1000 copies/ml. No patients from ZLE regimen had viral load above 1000 copies/ml. Widely used SLN regimen patients had viral load ranging from 1042 copies/ml to 31,13,018 copies/ml[13].

SUMMARY AND CONCLUSION
- In this study , 159 HIV positive patients who were on ART were observed .Age, sex and baseline CD4 count was matched.Increase in CD4 count was more in ZLN group followed by SLN group followed by ZLE group. Anemia was seen in 7.55% of patients on ART but there was no correlation between anemia and the ART

regimen.Transaminitis was seen in 7.55% of patients studied, all of whom were on regimens containing nevirapine.Dyslipidemia was seen in 6.29% of the studied patients but there was no correlation with the ART regimen.Skin Rash was seen in 6.92% patients all of whom were on Nevirapine based regimens[1]. Thus we conclude for all three antiviral regimens tested, higher increase in CD4 count after 6 month of ART was 68.03% in ZLN group.

Table No 1 : Distribution of sex as per ART regime

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Study Group		SEX		Total
		Male	Female	
ZLN	Count	34	26	60
	Percent	56.7%	43.3%	100.0%
SLN	Count	32	22	54
	Percent	59.3%	40.7%	100.0%
ZLE	Count	26	19	45
	Percent	57.8%	42.2%	100.0%
Total	Count	92	67	159
	Percent	57.9%	42.1%	100.0%
Chi-Square t Study	Value	df	P value	Association is
Pearson Chi-Square	0.079	2	0.961	Not significant

Distribution of study group as per ART Regime were ZLN-37.74%, SLN-33.96%, ZLE-28.30%.

Table No 2:Comparison among study group for Baseline CD4 count

| CD4 Count Baseline	N	Mean	Std Dev	Median	IQR	Kruskal-Wallis test applied	
ZLN	60	246.6	28.29	248.5	50.5	H value	P Value
SLN	54	251.3	25.85	249	37.25	1.500	0.470
ZLE	45	253.3	26.36	256	44	Not significant	
Note : Normality Test (Shapiro-Wilk) Failed (P < 0.050), thus Kruskal-Wallis One Way Analysis of Variance on Ranks test applied.							

ZLN-246.6%, SLN-251.3%, ZLE-253.3%.

8] Table No 3
Comparison among study group for cd4 count at 6 month

CD4 Count at 6 mths	N	Mean	Std Dev	Oneway ANOVA test	
ZLN	60	314.65	52.401	F value	P Value
SLN	54	300.54	45.294	5.474	0.005
ZLE	45	282.36	50.324	Significant	

ZLN-314.65%, SLN-300.54%, ZLE-282.36%. Average increase in CD4 count after 6 month of ART was 68.03 in ZLN group; 49.26 in SLN group and 29.09 in ZLE group. The difference of average increase in CD4 count after 6 month of ART was statistically significant in the three groups

Table No 4

Distribution of adverse effects as per ART regime
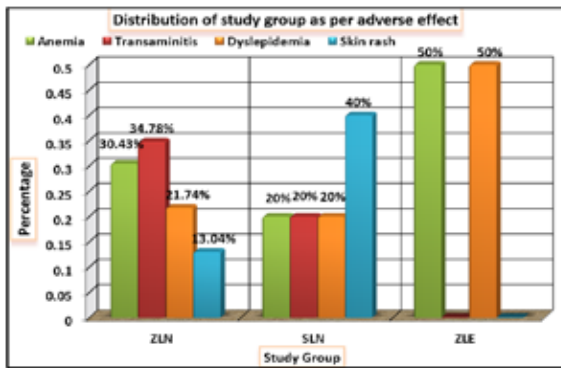
Maximum reaction was seen in ZLE regime followed by SLN and ZLN .Anemia was seen in 50%in regimes with ZLE followed by ZLN .Transaminitis was highest in ZLN regime and skin rash associated with nevirapine seen in group SLNand ZLN .

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