



INCREASE IN CD4 COUNT AFTER INITIATION OF SECOND LINE ANTI-RETROVIRAL THERAPY

Dr Aditya D Phadte*

Department of Medicine, Goa Medical College, Bambolim Goa, India. *Corresponding Author

Dr Prithvi K A

Department of Medicine, Goa Medical College, Bambolim Goa, India.

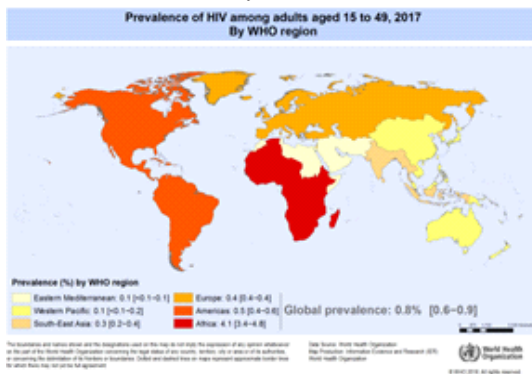
ABSTRACT Worldwide, there are 17 million people living with HIV/AIDS (as per GLOBAL AIDS UPDATE 2016). Increasing number of patients are needing second line anti-retroviral therapy. To address and prepare for this scenario, critical assessment of outcomes of second line anti-retroviral therapy are relevant. We are evaluating immunological outcomes of second line ART among HIV infected individuals seeking treatment in Goa Medical College ART center.

KEYWORDS : HIV/AIDS, second line anti-retroviral therapy, immunological outcomes

INTRODUCTION

HIV Infection and AIDS Worldwide:

HIV infection/AIDS is a global pandemic. At the end of 2013, estimated 35 million individuals were living with HIV infection according to joint United Nations Programme on HIV/AIDS (UNAIDS). An estimated 95% people living with HIV/AIDS live in low/middle income countries; approximately 50% are female and 3.2 million are children less than 15 years.



Picture 1: HIV burden in various parts of the world in adults aged 15-49 years¹

HIV treatment principles and guidelines:

As the biology of HIV virus is understood better and different classes of potent drugs are developed, it is now mandatory to employ highly active anti-retroviral therapy (HAART) which is the combination of ≥ 3 drugs.

First line regimens of ART universally include 2 Nucleoside Reverse Transcriptase Inhibitors (NRTIs) + 1 Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI).

Some principles of 1st line regimens:

- 2 NRTIs + 1 NNRTI
- Include lamivudine in all regimens
- Other NRTI can be zidovudine/ stavudine
- Choose one NNRTI from nevirapine or efavirenz
- Choose efavirenz in patients with hepatic dysfunction and patient concurrently receiving rifampicin.
- Choose nevirapine in pregnant women.

First line anti retroviral regimens:

- Preferred:
Lamivudine + Zidovudine + Nevirapine
- Alternatives:
Lamivudine + Zidovudine + Efavirenz
Lamivudine + Stavudine + Efavirenz
Lamivudine + Stavudine + Nevirapine
- Others:
Lamivudine + Tenofovir + Nevirapine

- Lamivudine + Tenofovir + Efavirenz
- Lamivudine + Zidovudine + Tenofovir

Definitions of treatment failures for 1st line ART:²

Clinical failure:

New or recurrent WHO stage IV condition after at least 6 months of effective treatment.

Immunological failure:

- Fall of CD4 count to pre therapy baseline (or below) OR
- 50% fall from the on treatment peak value OR
- Persistent CD4 levels < 100 cells/mm³.

Virological failure:

Plasma viral load > 1000 copies/ml.

Failure is usually due to development of resistance to one or more drugs of a particular regimen and is inevitable, hence should be anticipated. Once a regimen is failed, all 3 drugs should be changed and not only 1 or 2 of them.

Good adherence is the key to maintaining the first line ART for longer duration and for second line ART to ensure viral suppression and increase survival.

Some principles to design second line regimens:

1. Drugs which might develop cross resistance should be avoided.
2. A boosted PI (Protease Inhibitor) is almost always included in second line regimen.
3. As one of the NNRTIs is always there in first line and resistance to one means resistance to all NNRTIs, this class of drugs is not included.
4. After multiple regimens have failed, integrase inhibitor (raltegravir), CCR5 inhibitor (maraviroc) or fusion inhibitor (enfuvirtide) can be considered.

Second line regimens suggested by NACO:

NRTI component:

Standard regimens :

1. Tenofovir + Abacavir
2. Didanosine + Abacavir
3. Didanosine + Zidovudine
4. Tenofovir + Lamivudine

Special circumstances:

1. Didanosine + Zidovudine
2. Didanosine + Lamivudine

Protease Inhibitor component:

1. Lopinavir/r
2. Atazanavir/r
3. Saquinavir/r
4. Indinavir/r
5. Nelfinavir

AIM:

To assess increase in CD4 count in HIV patients after initiation of

second line anti-retroviral therapy.

MATERIALS & METHODS:

- This is a retrospective study analyzing data collected from ART center about details of patients who received second line ART for at least one year.
- CD4 count at the beginning of starting second line ART was compared with CD4 count done one year of completion of second line ART in patients who had good compliance to treatment.
- Data of 102 patients was analyzed by relevant statistical methods.
- Details about the identity of the patient was maintained strictly confidential.

INCLUSION CRITERIA:

- HIV positive individuals on second line ART.
- Minimum one year of treatment with second line ART.
- Good compliance to treatment (>80%).

EXCLUSION CRITERIA:

- Second line ART for less than one year.
- Poor compliance to treatment (<80%).

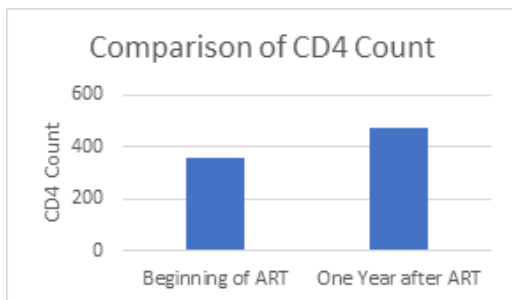
RESULTS:

Table 1 makes a comparison of CD4 count at the beginning of second line ART and 1 year of second line ART. SD= Standard deviation, SEM= Standard Error of the Mean

	Cd4 Count (in cells/mm3)		
	Mean	SD	SEM
At the Beginning of second line ART	361.45	313.59	31.05
After one year of Second line ART	476.98	321.83	31.86
Paired t Test, P Value <0.001, Significant			
Correlation Coefficient = 0.499			

Mean value at the beginning of second line ART was 361.45 cells/mm3, whereas after 1 year of second line ART it was found to be 476.98 cells/mm3 .

The mean increase in CD4 count was 115.53 cells/mm3. Statistical analysis done by paired t test yielded a p value <0.001 which was significant.



Picture 2: Bar chart showing comparison of mean value of CD4 count (cells/mm3) at the beginning of second line ART and one year after second line ART

DISCUSSION:

With an increase in number of HIV patients; there is an increasing trend for patients on second line ART.

In our study, we planned to assess efficacy of second line ART by comparing the CD4 count at the beginning of second line ART and 1 year after starting second line ART.

At the time of initiation of second line ART, CD4 count was lower as observed in other studies done by Jha et al³ and studies done in South Africa.^{4,5} The CD4 count was more in the study done in South Africa⁵ as compared to our study. It may be because old National AIDS Control Organization (NACO) guidelines⁶ defined virological failure with plasma viral load more than 10,000 copies/ml, while in South Africa this is defined as viral load >1000 copies/ml.

However in the recent NACO guidelines of October 2018, virological failure is defined by plasma viral load > 1000 copies/ml.²

There was an increase in CD4 count at the end of 1 year of starting second line ART as seen in other studies.^{3,7,8,9}

LIMITATIONS:

Limitations of the study were small sample size and absence of viral load for comparison. A large scale prospective study may be done for overcoming limitations.

CONCLUSION:

There is an obvious immunological improvement in patients who are on second line ART when they are followed up over a period of 12 months.

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