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A Study on Toxicity and Tolerability of Tenofovir in Tenofovir based First Line Anti Retroviral Therapy in ART Naïve Patients

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1. Introduction & Background

Tenofovir has been recently introduced in our country as first line therapy in HIV infection but limited data available on safety profile (special concern is its association with nephrotoxicity) tolerability in Indian population of patients.

The main concern is Nephrotoxicity of Tenofovir and the study will focus on toxicity, particularly nephrotoxicity & tolerability of Tenofovir in Tenofovir based 1st line ART regimens as none of the other drugs in these regimens are Nephrotoxic.

2. Methods

We took approval from Institutional ethics committee & Informed consent from all the study subjects. We studied subjects from July to December 2014 and followed up of each for 6 months, collected detailed history did physical examinations and baseline investigations before initiation of ART and subsequently at 2weeks, 1 month, 3 month and 6 month of starting of ART. We assessed tolerability to the regimens by symptoms of patients (nausea, vomiting, loss of appetite etc) and laboratory tests report. We collected all data data & analyzed by using SPSS.

3. Discussion

HIV infection causes significant morbidity and mortalityby causing an immune deficient state and patients usually succumb to death from unusual opportunistic infections and malignancies. However HIV infection is a manageable with HAART. We conducted the study involving 97 eligible patients who were followed up for a period of 6 months. We studied toxicity and tolerability of tenofovir.

We observed gastrointestinal intolerance which includes anorexia, nausea, vomiting and upper abdominal pain in 12.37% patients at 2 weeks of starting of ART which subsequently relieved with time. Only 4% patients had GI intolerance at 1 month which relieved after few days. We found that there is increment in mean haemoglobin level of total study population from base line value. There was no effect on mean total and differential leucocyte count and also on the mean platelet count.

We found no adverse effect of the drug on liver function (serum bilirubin, SGOT, SGPT did not show any change).

The study showed that there is increasing value of mean serum creatinine level of total study population from base line value but mean serum creatinine at the end of study remained within normal reference value. None of the study population developed acute renal failure or feature of proximal renal tubular dysfunction (glycosuria in presence of normal plasma glucose and proteinurea) for which discontinuation of tenofovir required. The pattern of change in serum creatinine level is same in both sex group.

We also found that there was increasing value of mean serum urea level of the total study population from base line value although the value at the end of study remained within normal reference value.

We found there is clinical, biochemical and improvement of overall health in general of the study population probably due to well control of the disease and also the control of opportunistic infection. The study population had overall weight gain at the end of the study

4. Results

This study shows that tenofovir is well tolerated drug in this population of patients with once daily regimen which has improved patients compliance. Tenofovir therapy improves overall general health of the patients.Tenofovir therapy is associated with mean weight gain and increased in haemoglobin level. It is not associated with adverse effect on total leucocyte count, differential leucocyte count, platelet count, serum bilirubin and serum liver enzymes (SGOT, SGPT). Within this 6 month follow up, evidence of nephropathy or proximal renal tubulopathy is not seen in any study subject.

5. Conclusion

Tenofovir is well tolerate and very safe drug in these patients without prior renal disease and concurrent nephrotoxic drugs, the follow up of these patients should be done to know the exact incidence of nephropathy as literature has concerned us about the possibility of renal toxicity with tenofovir with prolonged exposure.

6. Ethical Considerations

The Institutional Ethics Committee of NBMCH approved for our study.

7. Acknowledgement

We are grateful and indebted to respected Principal Sir, MSVP Sir, Deputy Superintendent and Assistant Superintendents for being of help whenever needed.

8. Source of Funding

We expend from our personal account.

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Abbreviation

HIV- Human Immunodeficiency Virus.
SIV- Simian Immunodeficiency Virus.
AIDS- Acquired Immunodeficiency Syndrome.
AZT –Zidovudine.
HAART- Highly active antiretroviral therapy.
NNRTI -Non-nucleoside reverse trancriptase inhibitor.
TDF-Tenofovir disoproxil fumarate.
NACO-National Aids control organization.
ART-Antiretroviral therapy.
PrEP-Pre-exposure prophylaxis.
Sd- Standard deviation.
Hb-Haemoglobin.
TLC-Total leucocyte count.
DLC-Differential leucocyte count.
LFT-Liver function test.
ALT-Alanine transaminase.
NBMC-North Bengal medical college Diagram 1: Distribution of total study population according to age

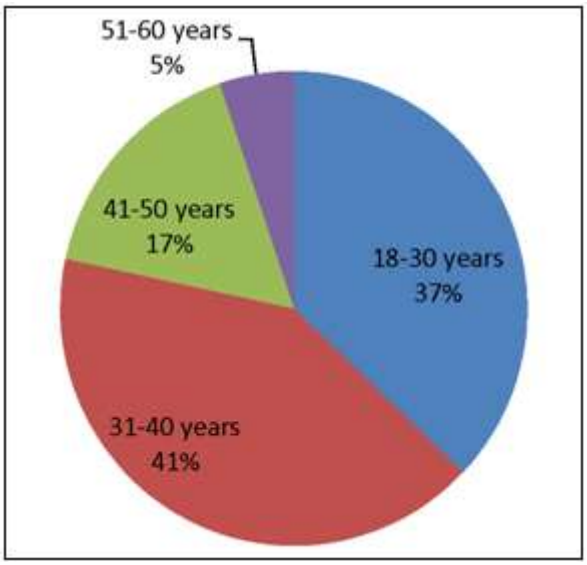
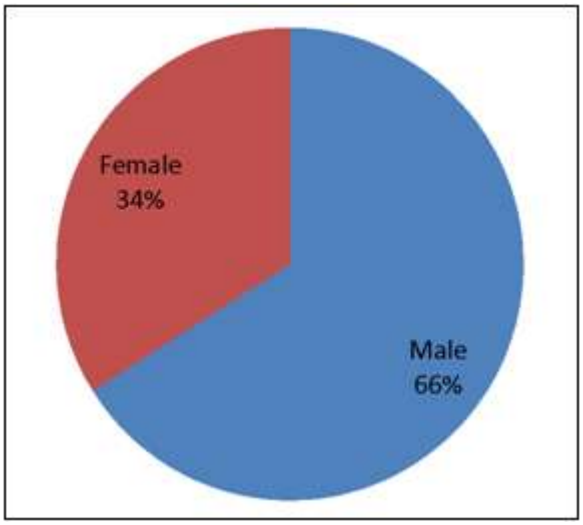


Diagram 2: Distribution of total population according to sex distribution



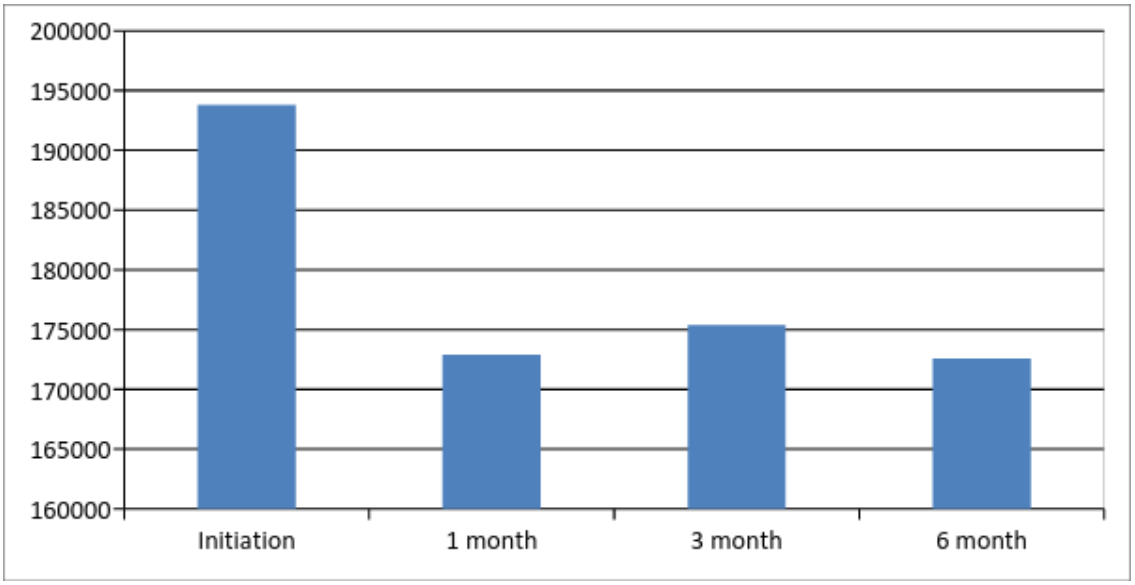


Figure 1: Change in platelet count (mean+/-Sd) of total study population observed during the study period.

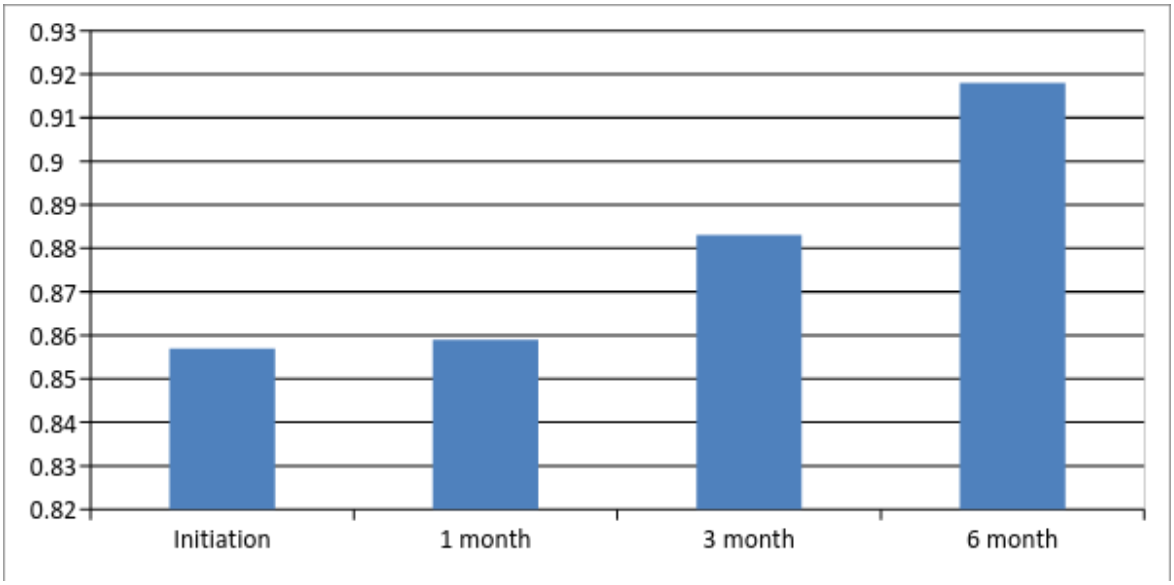


Figure 2: Change in mean serum creatinine level of total study population observed during the study period.

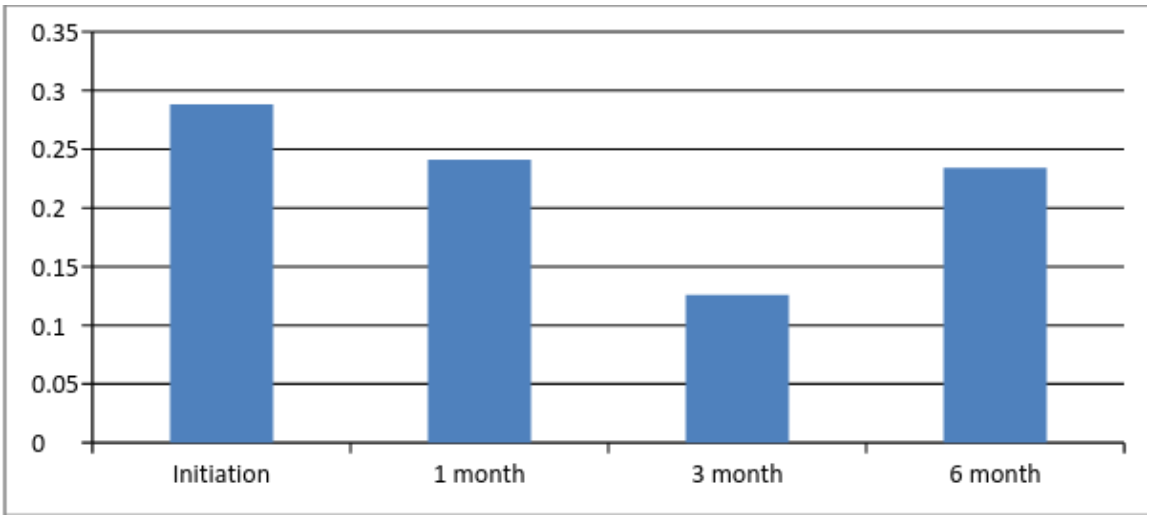


Figure 3: Change in serum direct bilirubin level (mean+/-Sd) of total study population observed during the study period .

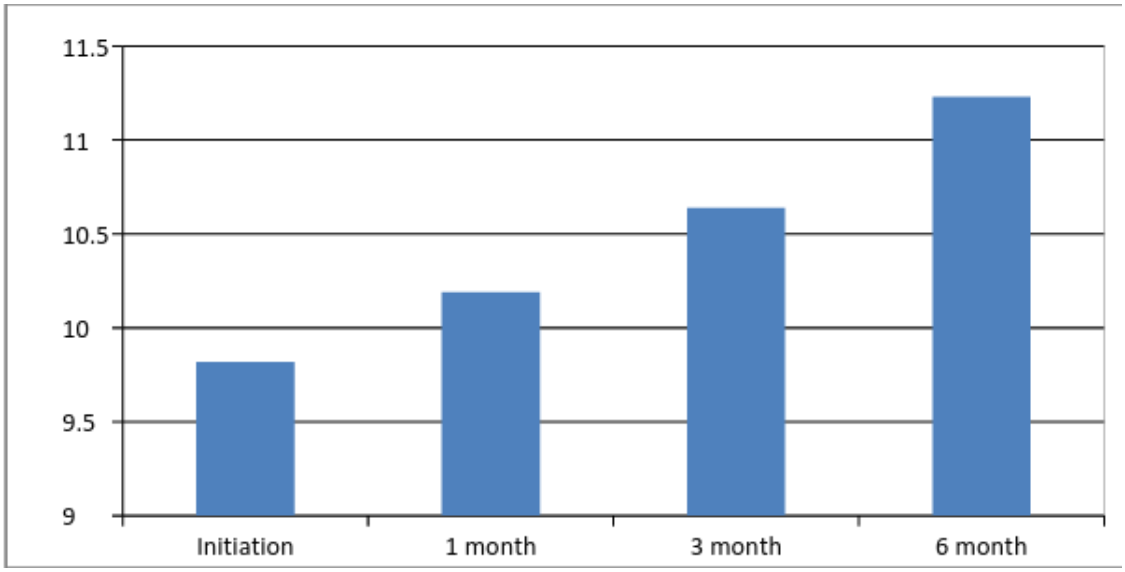


Figure 4: Changes in haemoglobin level (mean+/-Sd) of female population under study observed during study period.

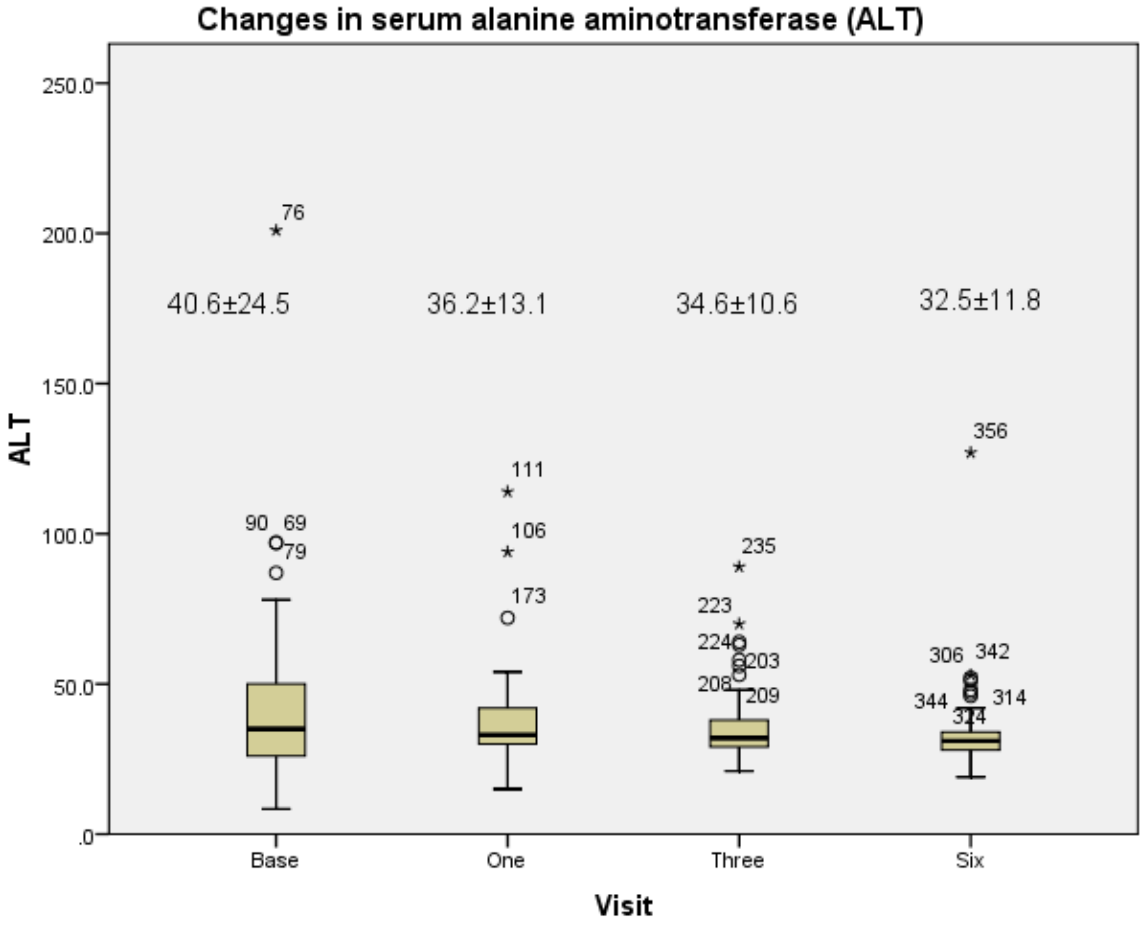


Figure 5: Changes in serum alanine aminotranferase

Table 1: Tenofovir and renal parameter

Parameter	At initiation	At 1 month	At 3 month	At 6 month
Serum Urea(mean+/-Sd)	21.431+/-5.21	20.784+/-3.14	21.928+/-3.14	22.928+/-3.7
Serum Creatinine(mean+/-Sd)	0.857+/-0.169	0.859+/-0.109	0.883+/-0.1	0.918+/-0.125
Urine for Protein	Trace in 5 pts	Nil	Nil	Nil
Urine for glucose	Present in 1 pts	Nil	Nil	Nil