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Efficacy and tolerance of TDF-3TC-EFV combination therapy in HIV 1 patients in a resource limited setting

Ndow G,[1] Diop SA,[1] Seydi M,[1] Fortes-Déguénonvo L,[1] Manga NM,[1] Dia NM,[1] Basse CD,[1] Ndour CT,[1] Soumare M,[1] Diop BM,[1] Sow PS[1]

[1]Department of Infectious Diseases & Tropical Medicine, FANN Teaching Hospital, Cheikh Anta DIOP University, DAKAR

Introduction

- Increasing number of patients are being started on tenofovir containing anti-retroviral (ARV) regimens in Senegal.
- Such combinations have been poorly studied in sub-Saharan Africa.
- We conducted a study to evaluate the efficacy and tolerance of the TDF-3TC-EFV combination regimen in HIV 1 patients.
- OBJECTIVES: To measure the efficacy of such combination in the management of infection with HIV 1, as well as to evaluate its tolerance.

Methodology

- A retrospective study between 2007 and 2011.
- All HIV 1 patients followed-up at the Regional Centre for HIV Research & Training (CRCF) and the Department of Infectious Diseases of the FANN Teaching Hospital receiving TDF-3TC-EFV either as first line ARV regimen or a switch treatment were included.
- Clinical and laboratory data was collected at initiation of therapy, at one month, and every six months subsequently.
- Data was analysed using Epi Info version 6.04

Results

Table 1: Characteristics of the study population

Variables	Value (N=100)
Sex M/F	53/47
Average age (yrs)	43.11±9.43
WHO Staging 1 – 2	12
WHO Staging 3	36
WHO Staging 4	52
Duration of follow-up	14.26 months [0-45.11]
ARV Treatment	
1st line	54
Switch	46
Compliance	
Good	85
Poor	15
SMX-TMP prophylaxis	73%
TB treatment	36%

- Average body weight at initiation was 53kg, with an average increment in body weight of 8kg per annum.
- Mean haemoglobin at initiation of therapy was 9.07g/dL, with 70.4% of population having Hb <10g/dL.

Table 2: Baseline measures

Variables		Percentage
Creatinine clearnce	>90mL/min	20
	60 – 89mL/min	50
	30 – 59mL/min	27
	<29mL/min	1
CD4 cell count (/mm³)	<50	26 (29.55%)
	50 – 200	27 (30.68%)
	>200	35 (39.77%)

- Mean CD4 count:
  - Initiation: 317 cells/mm³
  - 1-year treatment: 429cells/mm³
- Mean viral load
  - Initiation: 8,544copies/mL
  - 1-year treatment: 68copies/mL

Figure 1. Adverse drug reactions

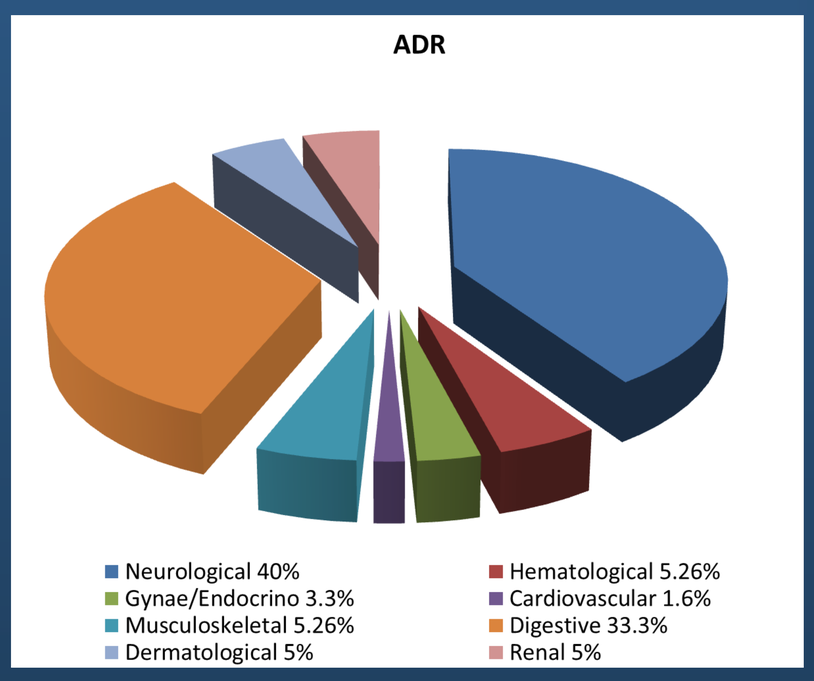

Table 3. Severity (grade) of undesired effects

ADVERSE REACTIONS	GRADE				TOTAL
	1	2	3	4	
Neurological	15	9	0	0	24
Dermatological	1	2	0	0	3
Hematological	0	2	0	1	3
Digestive	1	14	1	4	20
Musculoskeletal	1	1	1	0	3
Cardiovascular	1	0	0	0	1
Gynae/Endocrinology	0	1	0	0	1
Renal	0	0	2	1	3
TOTAL	19	29	4	6	58

- Apparition of ADRs was within the first 6months of treatment for >65% of patients
- Four patients had adverse effects severe enough to warrant change in their ARV regimen; three of these were a result of several renal insufficiency and the fourth was due to treatment failure (resistance to 3TC/EFV).
- There were thirteen deaths; 9males, 3females
  - WHO stages 3 or 4

Discussion

CLINICAL RESPONSE: The increase in body weight observed in this cohort tallies with findings of Kiertiburanakul et al, 2011 in Thailand (average weight of 56kg) and Landman R et al in Senegal (average weight of 58kg in females and 61kg in males). BMI could not be evaluated because a greater proportion of patients did not have their heights documented.

IMMUNE AND VIROLOGICAL RESPONSE: Similar results reported by Cassiti I et al in their 2007 study of patients on the same treatment protocol (TDF-3TC-EFV). Several other studies of efficacy and tolerance of TDF containing regimens report similar immunological and virological responses (Kiertiburanakul et al., 2011 , De Beaudrap 2010).

ADVERSE EFFECTS: Although common, most of the undesired drug reactions of the TDF-3TC-EFV combination are mild to moderate (Cassiti et al). The greater proportion were digestive and neuro-psychiatric, which is largely attributed to EFV. There is a potential risk of increased hepatic and neurological adverse effect with the combination of TDF and EFV (Lattuada E, 2008).

RENAL: The nephrological adverse effects are relatively rare and generally affect <5%, as also reported by Highleyman. It is more often is subjects with an underlying renal pathology (Rodriguez 2010; Gallant JE 2008). Patients often develop a progressive reduction in renal function (DeBeaudrap 2010; Gallant 2009).

Patients on this treatment protocol are at risk of developing Fanconi syndrome (Oundounda 2010, Gupta S, IAS 2011). We did not assess the occurrence of this problem in our study.

LIMITATIONS: The major limitation for this study was the inconsistent documentation of certain variables for all patients over the duration of follow-up.

Conclusion

Patients receiving TDF-3TC-EFV combination therapy need rigorous surveillance and periodic assessment of renal function because this combination although efficient, is not without significant adverse effects. There is the need for a large cohort prospective study.