

Weight evolution in patients after stavudine substitution for lipoatrophy in Rwanda: Comparison of zidovudine with tenofovir/abacavir



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Objectives

In patients manifesting lipoatrophy on stavudine-containing first-line antiretroviral treatment (ART) regimens in Rwanda, to a) assess weight evolution after stavudine substitution and b) verify if there was a significant difference in weight evolution if zidovudine or tenofovir (TDF)/abacavir (ABV) was used for substitution.

Analysis

Analysis of ART-outcomes in two urban government health centers (Kinyinya and Kimironko HC) in Kigali. All patients on stavudine-containing first-line regimens for an uninterrupted duration of minimal 6 months and substituting stavudine for lipoatrophy (diagnosed using a Lipodystrophy-Case-Definition-Study-based questionnaire) were included (N=116). The most severe cases replaced stavudine with TDF or ABV (N=40), the remainder with zidovudine (N=76). The weight evolution at 3, 6, 9 and 12 months after stavudine-substitution was recorded. Multivariate linear regression was performed to identify factors associated with the change in weight after substitution.

Table 1: Baseline characteristics of patients with lipoatrophy prior to substitution with stavudine

Baseline characteristic	Total (N=116)	TDF/ABV (N=40)	ZDV (N=76)	P-value
Sex				
Male	2 (1.7)	1 (2.5)	1 (1.3)	0.642
Female	114 (98.3)	39 (97.5)	75 (98.7)	0.952
Age (years) ^b	35.7 (32.3-38.6)	36.8 (34.3-39.9)	34.8 (32.1-38.1)	0.074
WHO clinical stage at baseline				
Stage 1	1 (0.9)	0 (0)	1 (1.3)	0.468
Stage 2	14 (12.1)	3 (7.5)	11 (14.5)	0.304
Stage 3	83 (71.5)	31 (77.5)	52 (68.4)	0.582
Stage 4	18 (15.5)	6 (15.0)	12 (15.8)	0.918
CD4 count before substitution (cells/ μ L) ^{b,c}	293 (196-370)	289 (222-367)	293 (192-370)	0.751
Time on ART (days) ^b	492 (406-632)	512 (400-596)	490 (417-669)	0.756
NNRTI				
NVP	96 (82.8)	36 (90.0)	60 (78.9)	0.891
EFV	20 (17.2)	4 (10.0)	16 (21.1)	0.305
Body weight at time of substitution (kg) ^b	60 (53-67)	61 (53-72)	60 (53-65)	0.440
Body weight loss prior to substitution (kg) ^b	3.0 (1.9-5.6)	3.3 (2.0-6.0)	3.0 (1.0-5.1)	0.248
Rate of weight loss (g/week) ^b	189 (115-280)	171 (111-326)	201 (125-257)	0.932
Secondary diagnosis of SH/LA				
No	102 (87.9)	31 (77.5)	71 (93.4)	0.385
Yes	14 (12.1)	9 (22.5)	5 (6.6)	0.019
Length of follow-up after substitution (days) ^b	342 (251-434)	398 (265-507)	337 (240-396)	0.018

^a data represent N (%) unless otherwise stated. ^b median (interquartile range). ^c within 6 months prior to substitution; missing for 5 individuals. TDF: tenofovir; ABV: abacavir; ZDV: zidovudine; WHO: World Health Organisation; ART: antiretroviral treatment; NNRTI: non-nucleoside reverse transcriptase inhibitors; NVP: nevirapine; EFV: efavirenz; SH/LA: symptomatic hyperlactatemia/lactic acidosis

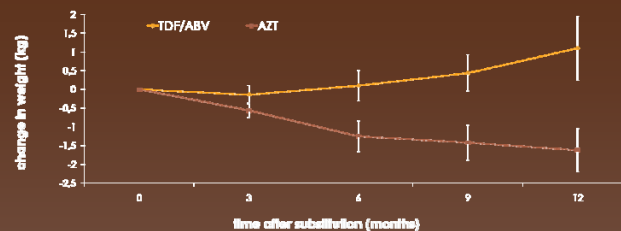


Figure 1. Weight evolution after substitution of stavudine for lipoatrophy (N=116). Data presented are the mean weight change and standard error of the mean (SEM).

Table 3. Multivariate analysis to assess the independent association of type of drug substitution with weight change^a

Baseline variables	Univariate analysis		Multivariate analysis	
	Coefficient	P value	Coefficient	P value
NRTI (ZDV vs TDF/ABV)	-1.994	0.010	-2.330	0.002
Time on ART	0.002	0.242	0.002	0.342
Sex	-3.770	0.177	-1.785	0.497
Age	-0.039	0.504	-0.041	0.455
WHO clinical stage (1/2 vs 3/4)	-0.070	0.949	-1.227	0.233
CD4 count before substitution	-0.002	0.441	-0.003	0.204
NNRTI (EFV vs NVP)	-0.857	0.376	-0.727	0.413
Body weight at time of substitution	-0.060	0.101	-0.065	0.083
Body weight loss prior to substitution	0.324	<0.001	0.455	0.002
Rate of weight loss	-0.004	0.086	0.004	0.268
Secondary diagnosis of SH/LA	-2.557	0.059	-2.081	0.132

^a Excluding 5 individuals with missing CD4 data (N=111);

Results

For those patients changed to zidovudine, a progressive weight loss was seen (mean loss by 12 months: 1.62 kg; P=0.001). In contrast, those on TDF/ABV displayed stable body weight, with a tendency towards recovery after an initial period of 3 months although this difference did not reach statistical significance. The between-group difference was significant from 6 months on (difference at 12 months: 2.7 kg, P=0.008). In multivariate analysis, substitution with TDF/ABV and pronounced weight loss prior to stavudine-change was significantly associated with weight gain.

Conclusions

This is the first study in Africa assessing "weight gain" as a proxy of recovery after substitution of stavudine for lipoatrophy. In this regard and although we do not know the metabolic implications of this finding, it might suggest that TDF/ABV is superior to zidovudine. The slow recovery of weight particularly with zidovudine highlights the need of alternatives for stavudine in first-line regimens, and the need of pro-active switching.

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