Weight loss after the first year of stavudine containing antiretroviral therapy and its association with lipoatrophy, virological failure, adherence and CD4 counts at primary health care level in Kigali, Rwanda

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Objectives

This study was conducted among 609 adults on stavudine-based antiretroviral treatment (ART) for at least one year at health center level in Kigali, Rwanda to a) determine the proportion who manifest weight loss after one year of ART b) examine the association between such weight loss and a number of variables namely: lipoatrophy, virological failure, adherence and on treatment CD4 count and c) assess the validity and predictive values of weight loss to identify patients with lipoatrophy.

Methods

Analysis of program data of 609 ART-naive adults on uninterrupted stavudine based ART for ≥1 year at two health centers in Kigali, Rwanda. Multivariate linear regression was used to identify key determinants of weight evolution: virological failure (viral load >1000 copies/ml), adherence, CD4 cell count, and lipoatrophy (using a Lipodystrophy-Case-Definition Study based questionnaire).

Results

Proportion of patients with weight loss after the first year on ART

We estimated that 61.9% of patients had a progressive decline in body weight (a negative slope) during the second year of treatment, with a calculated median slope of -3.1 kg/year (IQR -1.6;-5.6; $P < 0.01$). For those with stable or increasing weight, a median slope of +2.3 kg/year (IQR 0.8; 5.2; $P < 0.01$) was observed.

Association between weight loss and lipoatrophy, virological failure, ART adherence, and on-treatment CD4 count

The development of treatment-limiting lipoatrophy and lower on-treatment CD4 cell count were positively associated with weight loss after the first year of ART (Table 2). No significant associations were found with virological failure or treatment adherence.

Validity and predictive values of weight loss for identifying patients with lipoatrophy

We reasoned that, compared to transient weight changes, weight loss associated with the occurrence of treatment-limiting lipoatrophy would be persistent, progressive and/or chronic. Consequently, the association between the following indicators and lipoatrophy were explored: 1) weight loss occurring on at least two consecutive occasions relative to the "set-point" at six to 12 months after ART initiation, the period when weight appeared to stabilise in most patients, 2) progressive weight loss on at least two consecutive occasions with a minimal interval of one month, 3) weight loss occurring over a period of at least six months (Table 3). Sensitivity ranged from 29-100%; specificity varied between 58% and 93%. By combining different criteria, specificity could be improved, with a sensitivity and specificity of 75% and 93% for men, and 71% and 70% for women.

Conclusions

In a resource-limited setting, assessing weight is a routine clinical procedure that could be used to identify individuals at high risk of lipoatrophy after one year on stavudine-containing ART.

Table 2. Multivariate analysis to identify on-treatment determinants of weight change during the second year of treatment (kg) (N=609) [a]

	Univariate analysis		Multivariate analysis	
Variables	**Effect (kg/year)**	***P***	**Effect (kg/year)**	***P***
Lipoatrophy	-2.2 (-3.6;-0.8)	<0.01	-2.0 (-3.4;-0.6)	<0.01
Virological failure	0.9 (-0.9-2.7)	0.32	0.9 (-0.8-2.7)	0.29
Adherence to ART				
90-95% < vs 95-100%	0.3 (-0.8;1.4)	0.58	0.0 (-1.0;1.1)	0.93
< 90% vs 95-100%	0.7 (-0.4;1.9)	0.21	0.6 (-0.5;1.7)	0.41
CD4 cell count during 2nd year of ART(/100 cells/µL increase)	0.2 (-0.1;0.5)	0.18	0.4 (0.1;0.7)	0.01

[a] change (95% CI) in weight during second year of ART (kg/year); adjusted for age, sex, baseline WHO clinical stage and CD4 cell count, baseline weight, stavudine dose, non-nucleoside reverse transcriptase inhibitor used, weight change over the first year of treatment. ART: antiretroviral treatment

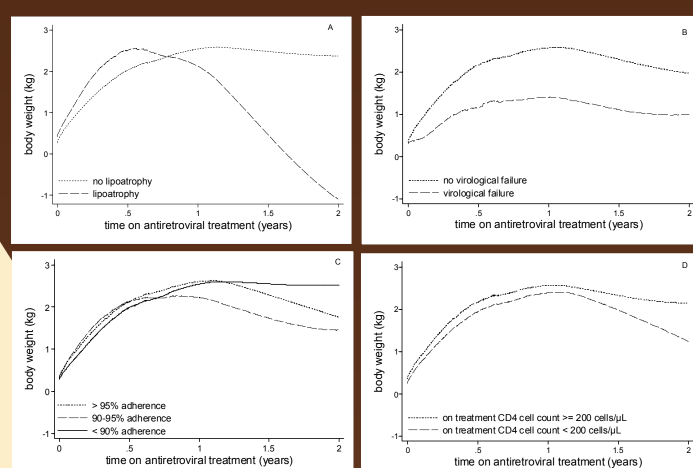

Figure. Weight evolution after initiation of stavudine-based antiretroviral treatment. The influence on weight evolution of the following on-treatment parameters is shown A. the development of treatment-limiting lipoatrophy during the 2nd year of treatment; B. the development of virological failure during the 2nd year of treatment; C. different treatment adherence levels; D. the mean CD4 cell count levels during the 2nd year of treatment. Mean values are given.

Table 1: Baseline and on treatment characteristics of adult ART naïve patients on d4T-based treatment regimens

Characteristic	Total (N=609)
Age (years) [b]	35 (31-41)
Female sex [a]	446 (73.2)
Baseline WHO clinical stage III/IV (vs I/II) [a]	467 (76.7)
Use of NVP (vs EFV) [a]	587 (96.4)
Stavudine dose 40 mg (vs 30 mg) [a]	138 (22.7)
Baseline body weight (kg)	
Female [b]	54 (54-59)
Male [b]	56 (52-62)
Baseline CD4 count (cells/µL) [b]	143 (81-206)
Weight increase over the 1st year of ART (kg) [b]	2.0 (-0.3;5.4)
CD4 cell count during 2nd year of ART(cells/µL) [b]	279 (188-398)
Lipoatrophy during 2nd year of ART [a]	74 (12.2)
Virological failure during 2nd year of ART [a]	44 (7.2)
Adherence to ART [a,c]	
95-100%	273 (44.8)
90-95%	172 (28.4)
< 90%	164 (26.9)

[a] data represent n (%)
[b] data represent median (interquartile range)
[c] based on pharmacy refill data
WHO: World Health Organization; ART: antiretroviral treatment; d4T: stavudine; NVP: nevirapine; EFV: efavirenz

Table 3. Sensitivity, specificity, positive and negative predictive values and area under the curve of specific patterns of weight evolution to detect lipoatrophy during the second year of treatment

MALE						FEMALE					
	Sensitivity	Specificity	PPV	NPV	AUC		Sensitivity	Specificity	PPV	NPV	AUC
Weight loss relative to the 'set-point' on ≥ 2 consecutive measurements with at least 1 month interval											
≥ 1 kg	4/4 (100%)	97/159 (61%)	4/66 (6%)	97/97 (100%)	0.80	≥ 1 kg*	51/70 (73%)	222/376 (59%)	51/205 (26%)	222/241 (92%)	0.66
≥ 2 kg	2/4 (50%)	130/159 (82%)	2/31 (7%)	130/132 (98%)	0.66	≥ 2 kg	27/70 (39%)	290/376 (77%)	27/114 (25%)	290/232 (86%)	0.58
≥ 3 kg*	2/4 (50%)	145/159 (91%)	2/16 (13%)	145/147 (99%)	0.71	≥ 3 kg	22/70 (32%)	327/376 (87%)	22/71 (32%)	327/375 (87%)	0.59
Progressively declining weight on ≥ 2 consecutive occasions with at least 1 month interval											
≥ 1 kg*	3/4 (75%)	130/159 (82%)	3/32 (9%)	130/131 (99%)	0.78	≥ 1 kg*	32/70 (46%)	290/376 (77%)	32/119 (28%)	290/327 (88%)	0.61
≥ 2 kg	2/4 (50%)	148/159 (93%)	2/13 (15%)	148/150 (99%)	0.72	≥ 2 kg	20/70 (29%)	346/376 (92%)	20/50 (40%)	346/396 (87%)	0.60
Weight loss occurring over a period of ≥ 6 months											
≥ 1 kg	3/4 (75%)	110/159 (69%)	3/52 (6%)	110/111 (99%)	0.72	≥ 1 kg*	52/70 (74%)	218/376 (58%)	52/210 (26%)	218/236 (92%)	0.66
≥ 2 kg	3/4 (75%)	124/159 (78%)	3/38 (8%)	124/125 (99%)	0.76	≥ 2 kg	39/70 (56%)	271/376 (72%)	39/144 (28%)	271/302 (89%)	0.64
≥ 3 kg*	3/4 (75%)	135/159 (85%)	3/27 (11%)	135/136 (99%)	0.80	≥ 3 kg	33/70 (47%)	305/376 (81%)	33/104 (33%)	305/342 (89%)	0.64
Combined criteria: two out of three criteria positive at 'optimal' cut-off											
	3/4 (75%)	148/159 (93%)	11/14 (21%)	148/149 (99%)	0.84		50/70 (71%)	263/376 (70%)	50/163 (32%)	263/284 (92%)	0.71

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