1H-MRS TO EVALUATE INTRAMUSCULAR LIPID CHANGES IN HIV-PATIENTS WITH LIPODYSTROPHY SYNDROME BY LCMODEL

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Introduction Lipodystrophy syndrome has been considered as a major problem for human immunodeficiency virus (HIV)-infected patients on antiretroviral drugs in the last years, which is characterized by subcutaneous fat wasting and intra-abdominal, breast or dorsocervical accumulation, dyslipidemia and insulin resistance. Highly active antiretroviral therapy has dramatically improved the long-term survival on HIV-infected patients, although it may play a role in the pathogenesis of this fat body changes, and the only intervention that has been shown to reverse lipoatrophy is the discontinuation of thymidine analogues (TA) (1,2). Since several studies have demonstrated an intramyocelular lipid (IMCL) accumulation measured by ^{1}H-MR spectroscopy (^{1}H-MRS) in this group of patients (3,4,5), we hypothesize that a probable muscle lipid mobilization may occur to peripheral fat after to switch the treatment.

Purpose Our aim was prospectively to investigate the lipid component in muscle in a group of HIV-infected patients with lipodystrophy and their changes with the lipoatrophy reversal after switching from TA to tenofovir-DF (TDF) by localized ^{1}H-MRS.

Study Design Twenty-eight HIV-infected patients with moderate to severe lipoatrophy, receiving stable antiretroviral therapy including TA (14 AZT; 14 d4T) were prospectively switched to TDF while rest of the therapy remained unchanged. Ten healthy volunteers were recruited to evaluate lipid component in muscle right as patients.

Methods The Research Ethics Committee of the Institution approved the protocol. At baseline and 6 months body composition measurements were performed in patients: total body and major sub regions of fat and fat-free mass, and bone mineral density (BMD) of the lumbar spine and proximal femur by DEXA, and intra-abdominal visceral (VAT) and subcutaneous (SAT) fat areas on a single cross-sectional abdominal CT image at L4 with standard protocols (2). Scans were performed using a 1.5 T whole body scanner (Symphony; Siemens Medical Systems, Erlangen, Germany) with the right calf placed in a knee coil. ^{1}H-MRS was acquired using a 3.6 mL single voxel PRESS spectroscopy pulse sequence with water suppression (TR/TE=3000/30 ms, 128 average, 1024 data points, BW 1200 Hz) and automatic shimming. Unsuppressed water signal acquisition of the same voxel (60 average) was obtained for each scan. Voxel was placed in soleus and tibialis anterior muscles on axial T1-weighted SE image (TR/TE=400/18 ms, slice thickness 5 mm, gap 0 mm, matrix 128 x 128, NEX 1, FOV 280 x 220 mm) and screen captured with voxel overlays for voxel placement during the follow-up examination (6). Fitting of all ^{1}H-MRS data was performed using LCModel software (6.1-4A) applying eddy current correction and water scaling. We considered IMCL methylene protons peak at 1.3 ppm, due the adequate repeatability because the homogeneous distribution (7). We evaluate body composition measurements changes after switching to TDF and we correlated with the IMCL metabolite concentration, and we compared lipid component in muscle in both patients and controls. We applied in the statistical analysis the U-Mann Whitney and Willcoxon signed rank tests, and Spearman coefficient and binary correlations ($p<0.05$).

Results As expected, patients 6 months after switching to TDF a significant peripheral and total fat content increased measured by DEXA, although peripheral and total lean mass decreased significantly (table 1). These findings were related with decreased in IMCL in both muscles, although no significant ($P>0.05$) (table 2). Patients presented higher IMCL than controls at the baseline in both muscles, and controls presented slight increased IMCL in muscle after 6 months, although no significant ($P>0.05$) (table 3).

TABLE 1. Fat, lean and DMO median changes in HIV+ (6 months vs baseline)
Only significant p-values are showed.

Wilcoxon signd rank test for Variable	AZT P-value	D4T P-value	Global P-value
Arm fat	0.00061		
Trunk fat	0.04187		0.01041
Total Fat	0.02454		0.00744
Leg Lean	0.001221	0.047852	0.000070
Trunk Lean			0.04380
Total Lean	0.047852	0.008545	0.000497
DMO	0.04358		
DMO Col		0.02783	0.01116
DMO Fem		0.02539	0.01225
Leg+Arm Fat	0.01343		0.00846
Leg+Arm Lean	0.010742		0.000718

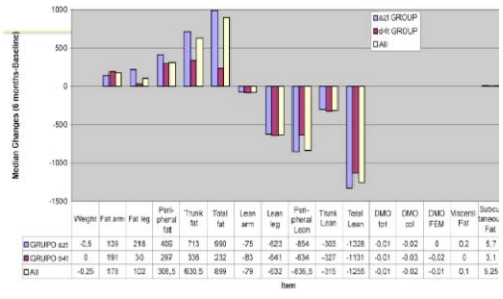

TABLE 2. IMCL changes by ^{1}H-MRS in HIV+ (6 months versus baseline)

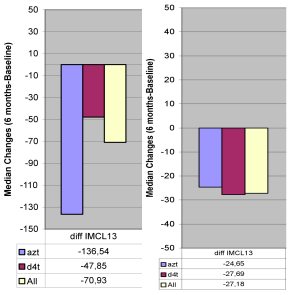

TABLE 3. Mean IMCL by ^{1}H-MRS in HIV-patients and controls baseline, 6 months, and changes 6 months versus baseline.

SOLEUS		HIV -	HIV +
IMCL130z	Mean	414.04	554.05
IMCL136z	Mean	464.70	536.64
diff IMCL13	Mean	20.91	-12.19

TIBIALIS ANTERIOR		HIV -	HIV +
IMCL130z	Mean	71.78	94.22
IMCL136z	Mean	88.15	84.68
diff IMCL13	Mean	11.71	-9.42

Conclusion After switching from TA to TDF leads to significant reversal of peripheral lipoatrophy, whereas lean mass decrease when measured by DEXA. Although we founded higher IMCL in patients than controls, and these decreased after 6 months, this was no significant. Our hypothesis of a probable relation between peripheral fat gain and loss of peripheral lean mass, with a decrease of IMCL probably related to migration of lipid content from intramyocellular to periphery, was not significantly confirmed. We point out IMCL can contribute, although other factors may participate.

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