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COPENHAGEN CO-MORBIDITY IN HIV INFECTION STUDY

REGION

LONG-LASTING ALTERATIONS IN FAT DISTRIBUTION IN PLWH EXPOSED TO THYMIDINE ANALOGUES

Poster number 0676

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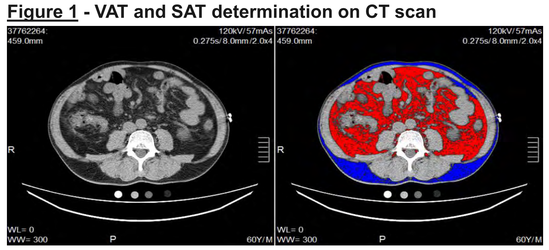
BACKGROUND

Thymidine analogues (TA) and didanosine (ddI) have been associated with redistribution of body fat from subcutaneous (SAT) to visceral (VAT) adipose tissue, which, in turn, is a risk factor for cardiovascular disease (CVD). We explored differences in adipose tissue distribution between people living with HIV (PLWH) with/without prior exposure to TA and/or ddI and uninfected controls and the association with CVD risk factors.

METHODS

761 PLWH from the COCOMO study aged > 40 and 2,283 age- and sex-matched uninfected controls from the GCPS study were included. PLWH were stratified according to prior exposure to TA and/or ddI. VAT and SAT were determined by abdominal CT-scan (Figure 1). Hypotheses were tested by linear and logistic regression analyses adjusted for age, sex, origin, smoking, physical activity, and BMI.

Figure 1 - VAT and SAT determination on CT scan



RESULTS

Age and sex distribution were similar in PLWH and uninfected controls (54.2 vs 54.4 years and 85.5% vs 85.5% male). 451 (60.5%) PLWH had exposure to TA and/or ddI. Of those, 6 (1.4%) were still exposed. Mean cumulative exposure was 6.6 (SD, 4.2) years and time since discontinuation was 9.4 (SD, 2.7) years. After adjustment, prior exposure to TA and/or ddI was associated with 21.6 cm2 larger VAT (13.8 –29.3) compared to HIV infection without exposure (Table 2). HIV-negative status was associated with similar VAT compared to HIV infection without exposure (Table 2). After adjustment, HIV infection with exposure to TA and/or ddI was associated with 14.8 cm2 smaller SAT compared to HIV infection without (-23.3 - -6.3). HIV-negative status was associated with 13.0 cm2 larger SAT compared to HIV infection without exposure (5.8 - 20.3) (Table 2). Cumulative exposure to TA and/or ddI (3.7 cm2 per year [2.3 - 5.1]), but not time since discontinuation (-1.1 cm2 per year [-3.4 – 1.1]), was associated with VAT (Table 3). In PLWH, prior exposure to TA and/or ddI was associated with excess risk of hypertension (aOR 1.62 [1.13 - 2.31]), hypercholesterolemia (aOR 1.49 [1.06 - 2.11]), and low HDL (aOR 1.40 [0.99 – 1.99]), when adjusting for confounders.

Table 2 - Linear Regression Model predicting the degree of change (with 95% CI) in cm2 of VAT and SAT

	Visceral adipose tissue				Subcutaneous adipose tissue			
	Unadjusted β* [95% CI]	p-value	Adjusted β* [95% CI]	p-value	Unadjusted β* [95% CI]	p-value	Adjusted β* [95% CI]	p-value
Study Group								
PLWH **without** exposure to TA/ddI	Ref		Ref		Ref		Ref	
Uninfected controls	17.6 [9.5;25.7]	< 0.0001	0.2 [-6.4;6.8]	0.9319	34.2 [24.1;44.3]	< 0.0001	13.0 [5.8;20.3]	0.0004
PLWH **with** exposure to TA/ddI	26.6 [16.8;36.3]	< 0.0001	21.6 [13.8;29.3]	< 0.0001	-15.6 [-27.8;-3.4]	0.0122	-14.8 [-23.3;-6.3]	0.0006
Age, per 5 years	10.6 [9.3;11.9]	< 0.0001	7.3 [6.31;8.4]	< 0.0001	-2.6 [-4.3;-0.9]	< 0.0001	-2.9 [-4.05;-1.7]	< 0.0001
Sex, male	43.9 [37.2;50.7]	< 0.0001	34.9 [29.3;40.5]	< 0.0001	-56.5 [-65.1;-47.9]	< 0.0001	-58.5 [-64.4;-52.5]	< 0.0001
BMI, per unit	9.1 [8.6;9.7]	< 0.0001	8.7 [8.2;9.2]	< 0.0001	14.8 [14.3;15.4]	< 0.0001	14.5 [13.9;15.0]	< 0.0001

*β coefficients represent the degree of change in cm^2 of VAT and SAT for every 1-unit of change in the explanatory variables.
Abbreviations: visceral adipose tissue, VAT; subcutaneous adipose tissue, SAT; people living with HIV, PLWH; thymidine nucleoside analog reverse-transcriptase inhibitors, TA; didanosine, ddI; body mass index, BMI; confidence interval, CI.
Multivariable models were adjusted for: age, sex, origin, physical activity, BMI, and study group

Table 1 - Demographic and clinical characteristics of the study populations

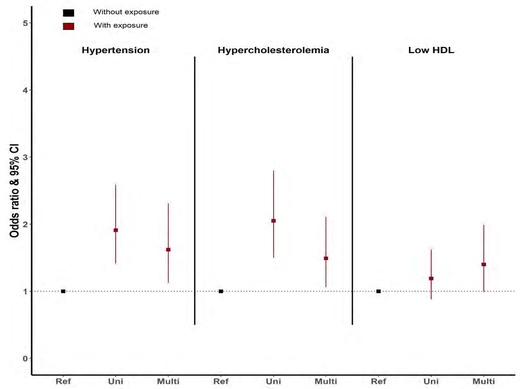
General characteristics	PLWH n = 761	Controls n = 2,283	p-value
Age, mean (SD)	54.2 (9.0)	54.4 (9.0)	0.594
Gender male, n (%)	651 (85.5)	1,953 (85.5)	1.000
Origin, n (%)			< 0.001
Scandinavia	570 (76.1)	2,122 (94.0)	
Other Europe	77 (10.3)	113 (5.0)	
Middle East and Indian sub-continent	12 (1.6)	18 (0.8)	
Other	90 (12.0)	4 (0.2)	
HIV Transmission mode, n (%)			
Heterosexual	166 (22.5)	-	-
IDU	9 (1.2)	-	-
MSM	516 (69.9)	-	-
Other	47 (6.4)	-	-
Current CD4 group, n (%)			
<200	13 (1.8)	-	-
200-349	50 (6.8)	-	-
350-500	116 (15.7)	-	-
>500	560 (75.8)	-	-
CD4 nadir < 200, yes, n (%)	337 (45.9)	-	-
cART, yes, n (%)	743 (99.8)	-	-
Current viral load < 50, n (%)	713 (96.2)	-	-
Years since HIV positive test, years, mean (SD)	16.0 (8.9)	-	-
Years since cART initiation, years, mean (SD)	12.1 (6.4)	-	-
Exposure to TA and/or ddI, n (%)	451 (60.5)	-	-
Present exposure, n (%)	6 (1.4)	-	-
Previous exposure, n (%)	445 (98.6)	-	-
Smoking status, n (%)			< 0.001
Never smoker	256 (34.3)	1,042 (46.0)	
Current smoker	196 (26.2)	275 (12.1)	
Ex-smoker	295 (39.5)	950 (41.9)	
Physical activity, n (%)			< 0.001
Inactive	68 (9.4)	114 (5.0)	
Moderately inactive	259 (35.7)	771 (34.0)	
Moderately active	310 (42.7)	1,099 (48.4)	
Very active	85 (12.3)	286 (12.6)	
Abdominal adipose tissue distribution			
VAT, cm^2, mean (SD)	104.4 (70.6)	106.5 (64.4)	0.456
SAT, cm^2, mean (SD)	140.7 (77.9)	184.8 (83.9)	< 0.001
VAT-to-SAT ratio, mean (SD)	1.0 (1.3)	0.6 (0.4)	< 0.001
BMI, mean (SD)	25.2 (3.9)	26.8 (3.9)	< 0.001

Abbreviations: People living with HIV, PLWH; visceral adipose tissue, VAT; subcutaneous adipose tissue (SAT); body mass index, BMI; standard deviations, SD; intravenous drug use, IDU; male-to-male sex, MSM, combined antiretroviral therapy, cART thymidine nucleoside analog reverse-transcriptase inhibitors, TA; hepatitis C virus, HCV

CONCLUSIONS

Prior exposure to TA and/or ddI was associated with long-lasting alterations in abdominal fat distribution, persisting after TA and/or ddI discontinuation, which may be involved in the excess risk of hypertension, hypercholesterolemia, and low HDL found in PLWH with prior exposure to TA and/or ddI. Our findings may help to identify a subgroup of PLWH who may benefit from more intensive monitoring and cardiovascular prevention interventions.

Figure 2 - Association between exposure to TA and/or ddI, hypertension, hypercholesterolemia, and low HDL



Association between exposure to thymidine analogues and/or didanosine and hypertension, hypercholesterolemia, and low HDL. Results from uni- and- multivariable logistic regression are reported as odds ratios (95% CI). Multivariable models were adjusted for exposure to TA and/or ddI, age, gender, smoking, physical activity, origin, and BMI. Abbreviations: people living with HIV, PLWH; thymidine nucleoside analog reverse-transcriptase inhibitors, TA; didanosine, ddI; body mass index, BMI; visceral adipose tissue area, VAT; confidence interval, CI.

Table 3 - Association between cumulative exposure to TA and ddI and VAT and SAT

	Visceral adipose tissue		Subcutaneous adipose tissue	
	Adjusted β [95% CI]	p-value	Adjusted β [95% CI]	p-value
Cumulative time of exposure to TA and/or ddI				
< 3.6 years	Ref		Ref	
3.6 – 6.3 years	17.5 [0.2;34.8]	0.047	-1.3 [-16.2;13.6]	0.862
6.4 – 9.2 years	40.8 [23.2;58.5]	< 0.001	7.6 [-7.6;22.8]	0.328
> 9.2 years	44.4 [26.0;62.7]	< 0.001	2.2 [-13.6;18.1]	0.781
Time since discontinuation of TA and/or ddI				
< 8.1 years	Ref		Ref	
8.1 – 9.6 years	-13.5 [-30.8;3.8]	0.127	8.1 [-6.8;23.1]	0.288
9.7 – 10.7 years	1.0 [-16.7;18.8]	0.906	-4.1 [-19.5;11.2]	0.595
> 10.7	8.62 [-9.4;26.7]	0.351	14.2 [-1.4;29.9]	0.075

*β coefficients represent the degree of change in cm^2 of VAT and SAT, respectively, associated with each level of the explanatory variables.
Abbreviations: visceral adipose tissue, VAT; subcutaneous adipose tissue, SAT; thymidine nucleoside analog reverse-transcriptase inhibitors, TA; confidence interval, CI.
All the models were adjusted for age, sex, origin, physical activity, smoking, BMI, cumulative time of exposure to TA and/or ddI, and time since discontinuation of TA and/or ddI

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