

Effects of Diet and Exercise and/or Rosiglitazone on Body Composition and Lipids including Oxidized LDL in HIV+ and HIV- Men and Women

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BACKGROUND

- Body-fat abnormalities, insulin resistance (IR), and lipid abnormalities are common in HIV+ adults on antiretroviral therapy (ART).⁽¹⁾
- Rosiglitazone (Rosi), an anti-diabetic drug, improves IR in HIV+ adults on ART, and Rosi is believed to improve body fat distribution.⁽²⁾
- Rosi is believed to increase risk of myocardial infarction and lipid abnormalities.^(3,4) This is especially a concern in a population who have increased cardiovascular disease risks, such as oxidized LDL (Ox LDL), due to HIV infection and ART use.⁽⁵⁾
- The following study is aimed at showing the effect of Rosi and lifestyle modifications on abnormalities common to HIV + patients on ART.

OBJECTIVES

- To study the *in vivo* effects of diet, exercise, and Rosi for 16 weeks on:
 - body fat distribution
 - lipids including Ox LDL (6)
- To compare the effects in HIV+ and HIV- people with aspects of the metabolic syndrome

METHODS

- 16 week, prospective, randomized trial
- HIV+ and HIV- men and women 20-60 yrs. of age, with waist circumferences >88.2 cm in men and >75.3 cm in women, fasting serum insulin \geq 16 μ U/ml, and BMI \geq 25
- Treatments:
 - Rosi (8 mg daily) alone
 - diet, exercise (promote loss of 2 lbs/week), & placebo (DEAP)
 - diet, exercise, & Rosi (DEAR)
- Measurements:
 - Body composition: whole body MRI & DEXA
 - Fasting lipids by standard methods
 - Ox LDL in frozen fasting plasma: competitive ELISA (Mercoxia, Sweden)⁽⁶⁾
- Data analysis:
 - Comparison of HIV groups: Student's t-test & Fisher's Exact Test
 - Treatment comparison: ANOVA with Tukey's HSD test for post-hoc analysis
 - Lipid results were controlled for smoking
 - Variables showing trends (P<0.20) for correlations were chosen for multiple regression analysis of Ox LDL
 - Data presented as mean \pm standard deviation
 - Significance level of p<0.05

RESULTS

- 32 subjects enrolled. 27 completed 16-week trial.
- Age: 44 \pm 9 years
- Sex, physical activity status, race, and age were not significantly different between HIV status or treatment groups.

Table 1. Baseline characteristics by HIV status

	HIV - (n=13)	HIV + (n=14)	P
Weight, kg	102.6 \pm 19.7	92.9 \pm 14.3	0.06
BMI, kg/m ²	35.9 \pm 6.5	31.6 \pm 4.7	0.05
Leg Fat, kg	14.5 \pm 6.3	8.9 \pm 4.3	0.01
Trunk Fat, kg	22.8 \pm 4.3	18.0 \pm 5.2	0.02
Total Fat, kg	42.9 \pm 12.0	31.3 \pm 10.3	0.01
Percent Body Fat (%)	0.49 \pm 0.11	0.34 \pm 0.13	0.09
Skeletal Muscle, L	29.1 \pm 6.9	29.7 \pm 6.3	0.98
Subcutaneous AT, L	41.6 \pm 17.0	32.9 \pm 9.9	0.49
Visceral Adipose Tissue, L	4.9 \pm 2.1	5.1 \pm 2.1	0.55
Ox LDL, U/L	63.0 \pm 21.8	66.0 \pm 19.7	0.24
LDL-Cholesterol, mg/dl	107.6 \pm 39.9	101.1 \pm 32.5	0.19
Ox LDL/LDL	0.02 \pm 0.01	0.02 \pm 0.01	0.97
Total Cholesterol, mg/dl	173.3 \pm 44.3	164.8 \pm 36.2	0.17
Triglycerides, mg/dl	128.9 \pm 70.0	143.5 \pm 66.2	0.69
HDL-Cholesterol, mg/dl	40.1 \pm 10.3	35.2 \pm 12.0	0.22

Randomization:				
	Rosi	DEAP	DEAR	
HIV-	n = 3	n = 6	n = 6	
HIV+	n = 4	n = 6	n = 5	

Table 2. Changes were not significantly different between HIV+ and HIV- except:

Treatment	Variable	HIV+	HIV-	p
Rosi	LDL	-11.3 \pm 12.6	17.4 \pm 13.4	.03
	Ox LDL	-13.7 \pm 8.7	3.5 \pm 15.4	.02
	leg fat	-14.3 \pm 8.7	-9.6 \pm 4.6	<.01
	trunk fat	-17.6 \pm 13.5	-13.5 \pm 10.3	.03
	total fat	-16.6 \pm 11.5	-10.4 \pm 8.1	.02
DEAP	% body fat	-14.6 \pm 14.7	-5.7 \pm 3.6	<.01
	Weight	-4.9 \pm 4.6	-4.0 \pm 4.5	.04
DEAR	BMI	-4.8 \pm 4.2	-2.6 \pm 4.1	<.01

Table 3. Biological and body composition changes by treatments.

	Rosi (n=5)	DEAP (n=12)	DEAR (n=9)	P ^b
Weight, kg				
Baseline	102.8 \pm 20.0	94.8 \pm 16.7	99.3 \pm 16.6	
Change	+1.7 \pm 1.4*	-5.6 \pm 3.6*	-4.8 \pm 3.9*	<0.01
BMI, kg/m²				
Baseline	35.5 \pm 6.3	32.8 \pm 3.7	34.5 \pm 7.0	
% Change	+2.1 \pm 2.3	-5.7 \pm 4.4*	-3.4 \pm 4.0	<0.01
Leg Fat, kg				
Baseline	15.1 \pm 8.7	10.1 \pm 5.1	11.8 \pm 3.6	
% Change	+12.6 \pm 10.6*	-12.5 \pm 7.4*	-3.0 \pm 8.0	<0.01
Trunk Fat, kg				
Baseline	22.6 \pm 5.2	19.7 \pm 3.6	21.3 \pm 4.5	
% Change	+9.2 \pm 6.1*	-16.0 \pm 11.9*	-5.3 \pm 7.5	<0.01
Total Fat, kg				
Baseline	44.0 \pm 16.0	34.5 \pm 9.0	37.8 \pm 9.4	
% Change	+7.3 \pm 5.1*	-14.1 \pm 10.3*	-4.2 \pm 5.7*	<0.01
Percent Body Fat (%)				
Baseline	0.47 \pm 0.13	0.37 \pm 0.10	0.41 \pm 0.12	
% Change	+3.8 \pm 5.9	-11.1 \pm 12.0*	-5.0 \pm 6.0*	0.02
SM Change, L	-0.5 \pm 1.7	-1.3 \pm 1.6*	-0.8 \pm 2.1	0.73
SAT Change, L	+0.8 \pm 1.8	-4.1 \pm 3.5*	-3.2 \pm 2.1*	0.01
VAT Change, L	-0.2 \pm 0.5	-0.6 \pm 0.7*	-1.1 \pm 0.9*	0.11
Oxidized LDL, U/L				
Baseline	56.9 \pm 16.1	64.6 \pm 22.7	71.8 \pm 20.5	
% Change	+16.5 \pm 23.6	-5.9 \pm 18.7	-12.2 \pm 17.2*	0.03
LDL-Cholesterol, mg/dl				
Baseline	102.6 \pm 21.3	100.3 \pm 38.3	114.2 \pm 42.3	
% Change	-1.7 \pm 18.7	-0.9 \pm 22.3	+8.3 \pm 71.6	0.89
Ox LDL/LDL				
Baseline	0.02 \pm 0.01	0.02 \pm 0.01	0.02 \pm 0.01	
% Change	+20.1 \pm 21.6	-3.0 \pm 21.4	-4.2 \pm 32.3	0.17
Total Cholesterol, mg/dl				
Baseline	128.9 \pm 85.9	165.2 \pm 41.3	178.5 \pm 48.8	
% Change	+5.6 \pm 16.1	-0.2 \pm 16.4	+4.6 \pm 42.2	0.90
Triglycerides, mg/dl				
Baseline	128.9 \pm 85.9	159.4 \pm 72.0	129.4 \pm 46.3	
% Change	+41.8 \pm 54.6	-9.4 \pm 39.1	-9.2 \pm 29.6	0.04
HDL-Cholesterol, mg/dl				
Baseline	38.0 \pm 9.5	33.1 \pm 10.6	38.8 \pm 11.6	
% Change	-4.0 \pm 18.1	+16.7 \pm 25.5	+3.1 \pm 17.2	0.15

* P<0.05 and [†] P<0.01 Baseline vs. Week 16 after treatment (two-sample paired t-test for comparison of means).[‡] P of analysis of covariance between groups.

- Change in triglycerides was the best predictor of Ox LDL, and was directly related (p = 0.02).

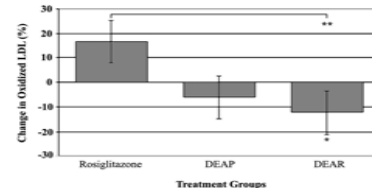


Figure 1. Percent change in oxidized LDL, by treatment group. DEAP, diet, exercise, and placebo; DEAR, diet, exercise, and rosiglitazone. Data shown as mean with standard error bars. *** Ox LDL change in DEAR group was significant. ** Ox LDL change in rosiglitazone group significantly different than DEAR. P<0.05 in significant.

DISCUSSION

- Baseline lipid panels, including Ox LDL, are not different in centrally obese, insulin resistant HIV- and HIV+ subjects.
- Rosi increased leg fat, trunk fat, and total body fat, but did not change VAT. The addition of diet and exercise reversed the increases in fat due to Rosi.
- There was a trend of increasing Ox LDL, Ox LDL/LDL and triglycerides from Rosi, and a significant decrease in Ox LDL from DEAR. The trends from Rosi may have been significant with a larger sample size.
- Body composition and lipid changes due to Rosi and DEAR were similar in people with and without HIV. The greater decrease in Ox LDL in HIV+ on DEAP may be reflective of greater compliance to the recommended diet and exercise, which is indicated by greater decreases in weight, BMI, leg fat, trunk fat, total fat, and % body fat in the HIV+ group compared to the HIV- group on DEAP.
- Rosiglitazone and Diet+Exercise have opposite effects. The effect of diet and exercise is stronger than the effect of Rosi.

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