Lipid lowering effects of rosuvastatin in HIV-infected patients on Highly Active Antiretroviral Therapy

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Introduction

- Highly active antiretroviral therapy (HAART) has transformed the human immunodeficiency virus (HIV) from a terminal disease to a manageable chronic disorder.
- Hyperlipidemia has become a common issue in the management of HIV due to factors, including the aging of our population, comorbid conditions, and the use of certain antiretrovirals, such as protease inhibitors (PIs) and efavirenz.[1,2,3]
- PIs are substrates and inhibitors of the cytochrome P450 (CYP450) system, particularly the CYP3A4 isoenzyme.[4,5]
- Most non-nucleoside reverse transcriptase inhibitors (NNRTIs) are also substrates and inducers of CYP3A4.
- Although most statins rely on CYP3A4 for elimination, rosuvastatin is primarily excreted unchanged in the urine.[5]
- A study pharmacokinetic in HIV-negative subjects coadministered rosuvastatin and lopinavir/ritonavir (LPV/RTV) demonstrated a blunted lipid-lowering response in spite of an unexpected increase in the plasma concentrations of the statin.[6]
- Moreover, there is no data on the efficacy of rosuvastatin in patients on NNRTI-based regimens.
- We conducted a retrospective analysis to evaluate the response to rosuvastatin in HIV-infected patients on either a PI-based or NNRTI-based regimen, and to compare the response of patients on different combination regimens.

Objectives

Primary Outcomes:

- Difference in total cholesterol (TC) and low density lipoprotein (LDL) serum concentrations after addition of rosuvastatin.
- Change in TC, LDL, and TC:HDL ratio among patients treated with varying antiretroviral regimens.

Secondary Outcomes:

- Difference in , triglyceride (TG) levels, high density lipoprotein ratio (HDL), and TC:HDL ratio after addition of rosuvastatin.

Methods

- Retrospective chart review of 83 HIV-infected patients treated at Saint Michael's Medical Center from March 2004 to October 2008.
- Inclusion criteria: patients ≥ 18 years of age, treatment with either a PI or NNRTI, concomitant treatment with rosuvastatin for at least 3 months, and a lipid profile drawn before and after rosuvastatin was initiated.
- Exclusion criteria: coadministration of other antilipemics, treatment with two PIs (excluding ritonavir) or a PI in combination with a NNRTI.
- Paired and unpaired Student's T-test was used to measure lipid changes among and between treatment groups.

Results

Table 1. Baseline Characteristics

	LPV/r arm n=12	FPV arm n=6	EFV arm n=8	Total N=26
Male sex, n (%)	6 (50)	4 (67)	5 (63)	15 (58)
Race, n (%)				
White	0	0	1 (12.5)	1 (4)
Black	8 (67)	6 (100)	1 (12.5)	15 (58)
Hispanic	4 (33)	0	6 (75)	10 (38)
Mean age, y	50	54	47	50
Mean CD4 cell count (cell/mm^3)	436	443	595	487
Mean Viral Load, n (%)				
< 50 copies/mL	2 (17)	1 (17)	0	3 (11.5)
< 400 copies/mL	5 (42)	3 (50)	7 (87.5)	15 (58)
≥ 400 copies/mL	5 (42)	2 (33)	1 (12.5)	8 (30.5)
Crestor dose, n (%)				
5 mg	1 (8)	0	0	1 (4)
10 mg	10 (83)	6 (100)	7 (87.5)	23 (88)
40 mg	1 (8)	0	1 (12.5)	2 (8)

N/n, number of patients; y, years; mm^3, millimeter; mL, milliliter; mg, milligram; r, ritonavir; LPV, lopinavir; FPV, fosemprenavir; EFV, efavirenz.

Table 2. Results – Overall Changes for all ARV regimens

	Baseline	3 months Post-Rosuvastatin	% Change	p-value
TC (mg/dL)	256	213	-16.8%	**0.013**
TG (mg/dL)	280	162	-42.1%	0.056
LDL (mg/dL)	151	114	-24.5%	**0.0035**
HDL (mg/dL)	57	61	+7.0%	0.57
TC:HDL	5.3	4.1	-22.6%	**0.032**

Table 3. Results – Comparisons Between ARV regimens

	EFV vs FPV	p-value	LPV/r vs EFV	p-value	LPV/r vs FPV	p-value
Δ in TC	-25.5 mg/dL	0.51	+52.48 mg/dL	**0.046**	+27.0	0.32
Δ in LDL	+6.5 mg/dL	0.86	+48 mg/dL	**0.05**	+54.6 mg/dL	0.082
Δ in TC:HDL	-0.32	0.85	-0.44	0.71	-0.76	0.46

Figure 1. Change in Total Cholesterol over 3 months

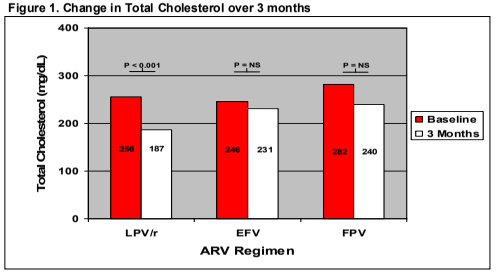


Figure 2. Change in LDL Cholesterol over 3 months

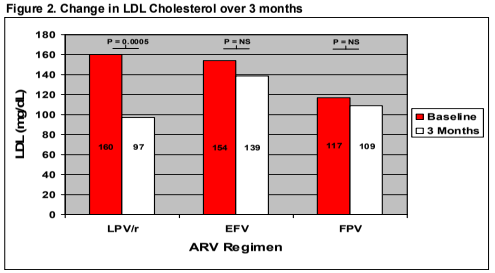
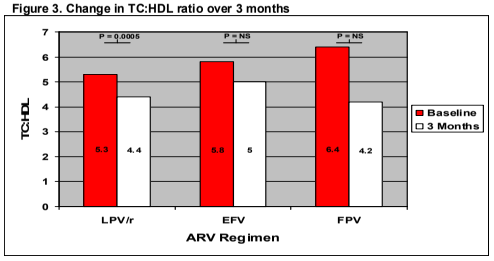


Figure 3. Change in TC:HDL ratio over 3 months



Discussion

- Rosuvastatin significantly decreased TC, LDL, and TC:HDL (16.8%, 24.5%, and 22.6%, respectively) in patients on HAART.
- LPV/r-treated patients had dramatic reduced lipid levels.
- TC and LDL values were lowered to a greater extent in patients treated with LPV/r versus EFV.
- No significant difference was found in the lipid-lowering effects of rosuvastatin between patients on FPV-containing regimens and patients on EFV or LPV.

Conclusions

- Rosuvastatin may have a role in the treatment of dyslipidemia in HIV-infected patients on HAART.
- Patients on LPV/r-based therapy appeared to received the greatest benefit from rosuvastatin.
- Larger studies are needed to determine whether there is an actual difference in the efficacy of rosuvastatin among different antiretroviral regimens.

References

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