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Dossier : Human and animal retroviruses

Cholesterol levels in HIV–HCV infected patients treated with lopinavir/r: Results from the SCOLTA project

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Abstract

Background: It is not known whether antiretroviral therapy (ART) including lopinavir/r has a different effect on the lipid metabolism in HIV patients co-infected with HCV. This study investigated changes in lipid levels, comparing patients with HIV infection alone and those with HCV too, in the lopinavir/r cohort of the SCOLTA project.
Methods: We analyzed the data for the lopinavir/r nationwide cohort from 25 Italian infectious disease departments, which comprises 743 HIV-infected patients followed prospectively, comparing subjects with HIV–HCV co-infection and those with single-infection.
Results: At enrolment, co-infected patients had significantly lower mean cholesterol than HCV negative cases (162 ± 43 mg/dL vs. 185 ± 52 mg/dL, $p = 0.0009$). Total and non-HDL cholesterol and triglycerides rose significantly from baseline in HIV single-infection patients, but not in those with co-infection. The patients with dual HIV–HCV infection, treated with an ART regimen including lopinavir/r, have only limited increases in total and non-HDL cholesterol and triglycerides.
Conclusions: Changes in serum lipids in co-infected patients differed significantly from those in patients without HCV. It remains to be seen whether this is associated with a lower risk of progression of atherosclerotic disease.

Keywords: Antiretroviral therapy; Lopinavir; HIV; Atherosclerosis; HCV; Cardiovascular diseases; Cholesterol; Lipids

1. Introduction

Patients with HIV infection receiving antiretroviral therapy (ART) may present a series of metabolic complications including blood lipid disorders, insulin resistance, lipodystrophy and a high incidence of metabolic syndrome [1–4]. The impact on lipid metabolism of protease inhibitors (PI), especially lopinavir/r, has raised questions about atherogenic potential and increases in cardiovascular pathologies [5–9]. However, recent studies have shown that high blood cholesterol in HIV patients receiving ART seems less marked when the patients also have

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HCV, like in people with HCV infection alone [10–16]. It is not clear, however, whether ART including lopinavir/r, the PI of first choice in most guidelines from developed countries, has a different effect on the lipid metabolism in HIV patients co-infected with HCV. Further, information about lipid changes after starting lopinavir/r, in patients outside of clinical trials, is scanty.

This study investigated changes in lipid levels, comparing patients with HIV infection alone and those with HCV too, in the lopinavir/r cohort of the SCOLTA project.

2. Methods

The SCOLTA (Surveillance Cohort Long-Term Toxicity of Antiretrovirals) project is an on-line nationwide pharmacovigilance program involving 25 Italian infectious disease departments. The SCOLTA project currently comprises seven cohorts: lopinavir, tenofovir, atazanavir, enfuvirtide, fosamprenavir, tipranavir and, very recently, darunavir. Data collection and follow-up procedures for the cohorts are described elsewhere [17].

We analyzed the data for the lopinavir/r cohort which comprises 743 patients followed prospectively. We excluded any patients for whom HCV serology (4.6%) or baseline blood cholesterol levels (23.3%), or both (2.3%), were not available. Patients were divided into two groups, HCV negative (HCV−) and HCV positive (HCV+). We recorded differences in total, non-HDL, and HDL cholesterol, triglycerides, and blood glucose at enrolment and at 6-monthly follow-up visits.

2.1. Statistical analysis

The SAS statistical package, release 8.2, was used for statistical analyses. Between-group differences in the percentages for categorical variables were tested by the Chi-square test, after adjustment for age according to the Mantel–Haenszel procedure. To evaluate the effects of other factors, differences between means were tested using analysis of covariance, fitting into the model variables known to be significantly associated with blood lipid levels.

The time from the start of lopinavir/ritonavir to development of hypercholesterolemia was analyzed with the Kaplan–Meier method; difference between the survival of HCV positive and negative patients was tested using the log rank test, accounting for age and gender. Patients with cholesterol level higher or equal to 240 mg/dL at enrolment were excluded from this analysis. A two-tailed p value less than 0.05 was considered significant.

3. Results

There were 519 evaluable patients (73.6% males, mean age 41 years ± SD 8) followed on the mean for 22 months (±SD 16). At enrolment the mean CD4 cell count was 286 cells/μL, and 3.5% had an undetectable viral load (<50 copies/mL); 37% had a diagnosis of AIDS and 18% were naïve to treatment. Characteristics of the 519 patients enrolled in lopinavir/ritonavir cohort according to HCV-status are shown in the Table 1. Serum HCV showed 282 negative (54.3%) and 237 positive (45.7%). The HCV− cases were older than the HCV+ ones (41.8 vs. 39.5 years), more often naïve to treatment (25% vs. 11.0%) and therefore with shorter pre-treatment times (47 vs. 74 months); and they had a higher viral load (log HIV-RNA 4.28 vs. 3.92). HCV+ patients were more likely to have acquired the disease through drug abuse (86.5% vs. 9.6%); they had significantly lower mean cholesterol at baseline than the HCV− group (162 ± 43 mg/dL vs. 184 ± 52 mg/dL, $p = 0.0009$). Non-HDL cholesterol was also lower in the HCV+ group than the HCV− patients (107 mg/dL vs. 126 mg/dL; $p = 0.05$). We found no real differences in baseline HDL cholesterol (57 ± 35 mg/dL vs. 59 ± 36 mg/dL), triglycerides (182 ± 112 mg/dL vs.198 ± 153 mg/dL) or blood glucose (92 ± 26 mg/dL vs. 91 ± 16 mg/dL).

In the course of the 6-monthly visits we noted increases in total and non-HDL cholesterol and triglycerides from baseline in patients with HIV mono-infection, but not in those with co-infection (Fig. 1 compares only total and non-HDL cholesterol). The differences between the two groups remained significant, however, after adjusting for age, sex, route of transmission of the infection, HIV-RNA, previous exposure to PI, or stavudine treatment at baseline or during follow-up. HDL cholesterol and blood glucose did not change noticeably in the two groups during follow-up (data not shown). During the lopinavir/ritonavir treatment, an increasing proportion of patients developed hypercholesterolemia (total cholesterol ≥ 240 mg/dL). After exclusion of patients who entered the study with such cholesterol levels, the probability of developing hypercholesterolemia (Fig. 2) was significantly higher in HCV negative than in HCV positive subjects ($p = 0.0009$, adjusted for age and gender).

Metabolic complications, including blood lipid abnormalities that led to withdrawal of ART arose in 6.4% of the HCV− and 4.2% of the HCV+ patients ($p = 0.27$). During follow-up 27 were HCV− and only nine HCV+ patients started blood lipid lowering treatment (crude $p = 0.02$).

4. Discussion

These findings indicate that patients with dual HIV–HCV infection, treated with an ART regimen including lopinavir/ritonavir, have only limited increases in total and non-HDL cholesterol and triglycerides. A previous study reports that a dyslipidemic pattern was more severe in subjects on PI-containing treatment, but HCV infection was not considered as confounding factor [18]. We showed that changes in serum lipids in co-infected patients differed significantly from those in patients without HCV. Similar results emerged from a recent study of Cooper et al. [14], which showed that co-infection with HIV and HCV should theoretically give less concern about ART causing lipid disorders, but did not address the specific influence of HCV on the lipid profile of lopinavir/ritonavir treated subjects.