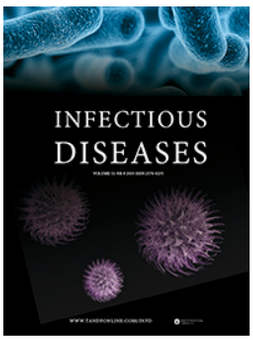

Infectious Diseases

ISSN: 2374-4235 (Print) 2374-4243 (Online) Journal homepage: https://www.tandfonline.com/loi/infd20

Efavirenz dose reduction is associated with improved lipid profile in HIV-1 infected patients

Stefano Nicolè, Massimiliano Lanzafame, Emanuela Lattuada, Dora Luise, Marta Vecchi, Evelina Tacconelli & Sandro Vento

To cite this article: Stefano Nicolè, Massimiliano Lanzafame, Emanuela Lattuada, Dora Luise, Marta Vecchi, Evelina Tacconelli & Sandro Vento (2019) Efavirenz dose reduction is associated with improved lipid profile in HIV-1 infected patients, Infectious Diseases, 51:8, 615-617, DOI: 10.1080/23744235.2019.1609078

To link to this article: https://doi.org/10.1080/23744235.2019.1609078

Published online: 12 May 2019.

Taylor & Francis
Taylor & Francis Group

INFECTIOUS DISEASES,
2019; VOL. 51,
NO. 8, 615–617

https://doi.org/10.1080/23744235.2019.1609078

LETTER TO THE EDITOR

Efavirenz dose reduction is associated with improved lipid profile in HIV-1 infected patients

To the Editor,

Recently in this journal, detailed Swedish recommendations on antiviral treatment of HIV infection were published, including management of adverse effects of the therapy [1]. We here contribute with our experience on a beneficial effect of Efavirenz dose reduction on the lipid profile.

Efavirenz is still extensively prescribed at the fixed dose combination of 600 mg with tenofovir disoproxil fumarate and emtricitabine (TDF/FTC) and is included in the World Health Organization's preferred first-line antiretroviral therapy (ART) for HIV-1 naive adults [2]. It has a proven virological efficacy but its use is associated with increases in serum lipid [3] and glucose levels [4] which appear to be directly related to the plasma levels of the drug [5].

In a phase 2, double-blind, placebo controlled, dose finding trial of efavirenz, 200, 400 and 600 mg of the drug plus 2 nucleotide analogue reverse transcriptase inhibitors (NRTIs) showed the same efficacy at week 24 in lowering HIV-RNA levels below 400 copies/mL in 137 patients randomly assigned to one of the three groups [6]. In the ENCORE-1 trial, a 400 mg dose of efavirenz was non-inferior and better tolerated compared to the 600 mg dose [7].

We have investigated the impact on the serum lipid profile of an efavirenz dose reduction from 600 to 400 mg/d and from 400 to 200 mg/d through an observational retrospective analysis on HIV1-infected patients followed at the Outpatient Infectious Diseases Unit of the G.B. Rossi University Hospital in Verona who reduced the dose of efavirenz between January 2010 and December 2017. We considered two groups; in the first, efavirenz was reduced from 600 to 400 mg daily (Group 1) and in the second, from 400 to 200 mg (Group 2). All patients signed an informed consent. In both groups, efavirenz was taken in combination with 2 NRTIs. All the patients had been virologically suppressed for at least 6 months before the dose was reduced, and none were taking lipid-lowering drugs, such as statins or fibrates, during the period examined. In each patient we compared fasting plasma values of total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides and glucose before efavirenz dose reduction and 12 months later. For statistical analysis we considered the mean values with standard deviations (SD) for all metabolic parameters. To compare the mean differences at the two different times we used 95% confidence interval and Student's *t*-test.

Forty-two patients switched efavirenz from 600 to 400 mg/d and 32 patients switched from 400 to 200 mg/d. Twenty-nine patients belonged to both groups as they reduced the dose of efavirenz from 600 to 400 mg first, and from 400 to 200 mg later. The characteristics of the two groups of patients are shown in Table 1. A significant reduction of total cholesterol levels was observed in both groups and of LDL levels in Group 2, whereas reduction of LDL levels in Group 1 was at the limit of statistical significance. Considering the data together and separating the patients in those on TDF ($n = 45$) *versus* those not on TDF ($n = 29$), we observed a mean reduction in total cholesterol of −8.5 mg/dL [CI: 95% −14.0,−3.0] in the TDF group *versus* − 10.3 mg/dL [CI: 95% −18.3,−2.3] in the non-TDF group, and a mean reduction in LDL of −5.9 mg/dL [CI: 95% −10.6,−1.2] in the TDF group *versus* − 7.6 mg/dL [CI: 95% −13.8,−1.2] in the non-TDF group. In the TDF group we observed a lower reduction in total cholesterol and LDL compared to the non-TDF group, but this difference is not statistically significant. All patients had been included also in two previously published reports on the virological efficacy of antiretroviral regimens including efavirenz at 400 mg [8,9] and 200 mg [8].

Table 1. General characteristics of study population, mean values of total cholesterol, HDL, LDL, triglycerides and glycemia before efavirenz reduction and after 12 months and mean differences in lipid and glucose serum values after 12 months from efavirenz dose reduction.

General characteristics	Group 1 ($n = 42$)		Group 2 ($n = 32$)	
Male (%)	31 (73.8%)		22 (68.8%)	
Median period of therapy with efavirenz before dose reduction in months (IQR)	43 (28–83)		43 (17–47)	
Median age at time of dose reduction in years (IQR)	44 (41–52)		48 (43–55)	
Backbone of 2NRTI. *n* (%)				
TDF/FTC	25 (59.5)		20 (62.5)	
ABC/3TC	14 (33.3)		9 (28.1)	
AZT/3TC	3 (7.1)		3 (9.4)	
Metabolic profile	Before reduction	After 12 months	Before reduction	After 12 months
Mean plasma total cholesterol in mg/dL (SD)	201.6 (39.1)	193.2 (36.9)	198.0 (45.0)	187.8 (29.8)
Mean change in total cholesterol in mg/dL [CI: 95%]	−8,5 [−14.5 to −2.4]		−10,2 [−17.3 to −3.1]	
p Value	$p<.01$		$p<.01$	
Mean plasma HDL in mg/dL (SD)	58.2 (19.0)	56.5 (18.8)	57.5 (15.3)	56.3 (15.6)
Mean change in HDL in mg/dL [CI: 95%]	−1.7 [−4.3 to 0.9]		−1.3 [−4.7 to 2.2]	
p Value	$p=.19$		$p=.23$	
Mean plasma LDL in mg/dL (SD)	118.9 (32.7)	113.3 (32.5)	119.2 (30.4)	111.3 (27.2)
Mean change in LDL in mg/dL [CI: 95%]	−5.6 [−10.6 to −0.6]		−7.8 [−13.5 to −2.2]	
p Value	$p=.03$		$p<.01$	
Mean plasma triglycerides in mg/dL (SD)	120.5 (64.9)	116.7 (57.3)	113.1 (52.3)	99.1 (29.5)
Mean change in triglycerides in mg/dL [CI: 95%]	−3.8 [−21.4 to 13.9]		−14.0 [−30.5 to 2.54]	
p Value	$p=.67$		$p=.09$	
Mean plasma glucose in mg/dL (SD)	91.8 (9.17)	92.5 (9.7)	91.6 (10.0)	90.9 (10.6)
Mean change in glucose in mg/dL [CI: 95%]	0.7 [−3.9 to 2.6]		−0.7 [−4.3 to 2.9]	
p Value	$p=.68$		$p=.70$	

IQR: inter-quartile range; SD: standard deviation; 95% CI: 95% confidence interval; ABC: Abacavir; AZT: Zidovudine; 3TC: Lamivudine; TDF: Tenofovir; FTC: Emtricitabine.

Our results show a significant decrease in total cholesterol levels when the dose of efavirenz is reduced to 400 or 200 mg. The statistically non-significant lower reduction of total and LDL cholesterol observed in the patients on TDF compared to those not on this drug is probably due to the known lipid lowering effect of TDF [10]. Our results are in keeping with those of Sinxadi et al. who showed an association between efavirenz concentrations and plasma lipid levels [5]; however, the mean changes in HDL, triglyceride and plasma glucose levels were not significant in our cohort.

In conclusion, a reduced dose of efavirenz (a 400 mg dose is now recommended as an alternative first-line regimen also by WHO [2]) can lead to a significant decline in total cholesterol and LDL and should be used especially in patients with cardiovascular or metabolic co-morbidities.

Disclosure statement

No potential conflict of interest was reported by the authors.

References

[1] Eriksen J, Albert J, Blaxhult A, et al. Antiretroviral treatment for HIV infection: Swedish recommendations 2016. Infect Dis (Lond). 2017;49:1–34.

[2] World Health Organization. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2016. Available from: http://www.who.int/hiv/pub/guidelines/arv2016/download/en/

[3] Fontas E, van Leth F, Sabin CA, D:A:D Study Group, et al. Lipid profiles in HIV-infected patients receiving combination antiretroviral therapy: are different antiretroviral drugs associated with different lipid profiles? J Infect Dis. 2004;189:1056–1074.

[4] Dave JA, Lambert EV, Badri M, et al. Effect of nonnucleoside reverse transcriptase inhibitor-based antiretroviral therapy on dysglycemia and insulin sensitivity in South African HIV-infected patients. J Acquir Immune Defic Syndr. 2011;57:284–289.

[5] Sinxadi PZ, McIlleron HM, Dave JA, et al. Plasma efavirenz concentrations are associated with lipid and glucose concentrations. Medicine (Baltimore). 2016;95:e2385.

[6] Gallant J, Seekins D, Hicks C, et al. A phase II, double-blind, placebo-control, dose-ranging study to assess the antiretroviral activity & safety of efavirenz (EFZ, sustiva, DMP266) in combination with open-label zidovudine (ZDV) w/lamivudine (3TC) at >48 weeks. [DMP266-005]. Intersci Conf Antimicrob Agents Chemother. 1998;24–27:38–441.

[7] ENCORE1 Study Group, Carey D, Puls R, Amin J, et al. Efficacy and safety of efavirenz 400 mg daily versus 600 mg daily: 96-week data from the randomised, double-blind, placebo-controlled, non-inferiority ENCORE1 study. Lancet Infect Dis. 2015;15:793–802.

[8] Lanzafame M, Bonora S, Lattuada E, et al. Efavirenz dose reduction in HIV-infected patients. HIV Med. 2012;13: 252–253.
[9] Lanzafame M, Lattuada E, Cucchetto G, et al. Efavirenz dose reduction in HIV-infected patients: a long-term follow-up. AIDS. 2014;28:2789–2790.
[10] Santos JR, Saumoy M, Curran A, et al. Randomized, cross-over, double-blind, placebo-controlled trial to assess the lipid lowering effect of co-formulated TDF/FTC. J Int AIDS Soc. 2014;17(4):19550.

Stefano Nicolè
Infectious Diseases Unit, Policlinico G.B. Rossi, University Hospital, Verona, Italy
stefano.nico.87@gmail.com

Massimiliano Lanzafame
Unit of "Diagnosis and Therapy of HIV Infection", Infectious Diseases Unit, G.B. Rossi University Hospital, Verona, Italy

Emanuela Lattuada, Dora Luise, Marta Vecchi and Evelina Tacconelli
Infectious Diseases Unit, Policlinico G.B. Rossi, University Hospital, Verona, Italy

Sandro Vento
Faculty of Medicine, University of Puthisastra, Phnom Penh, Cambodia

Received 29 March 2019; revised 12 April 2019; accepted 15 April 2019