International Journal of Infectious Diseases 17 (2013) e1259–e1262

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Short Communication

African ethnicity can influence immunological responses to highly active antiretroviral therapy and immunological success at 48 months: a retrospective pilot study☆

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ARTICLE INFO

Article history:
Received 23 April 2013
Received in revised form 1 August 2013
Accepted 3 August 2013

Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
CD4 recovery
HAART
HIV
African patient
Ethnicity

SUMMARY

Objective: To assess whether African ethnicity is independently associated with a poorer CD4 reconstitution with highly active antiretroviral therapy (HAART) compared to Caucasian ethnicity.
Methods: We conducted a retrospective epidemiological study among 575 HIV-1-positive patients at our center and defined immunological success as the presence of blood CD4 lymphocyte counts >500 cells/mm^3 in more than 50% of the values collected from 6 to 48 months after beginning HAART. Patients displaying an HIV-1 viral load >200 copies/ml or more than one HIV-1 viral load between 20 and 200 copies/ml during follow-up, were excluded. Patients with baseline blood CD4 counts >500 cells/mm^3 were also excluded.
Results: Two hundred and eighty patients met the inclusion criteria and no exclusion criteria. After 48 months of HAART, blood CD4 lymphocyte counts were lower in Africans than in Caucasians: 449 (65–975) vs. 569 (131–1698) cells/mm^3 ($p = 0.02$). Immunological success was present in 142/220 (64.5%) Caucasians vs. 29/60 (48.3%) Africans ($p = 0.02$). African ethnicity was independently associated with the absence of immunological success (odds ratio 2.22, 95% confidence interval 1.097–4.504; $p = 0.02$) despite similar baseline blood CD4 counts (219 vs. 204 cells/mm^3, $p = 0.72$).
Conclusion: Our findings suggest that African ethnicity is independently associated with a poorer CD4 reconstitution during HAART than Caucasian ethnicity.

1. Introduction

Patients of African origin still bear the heaviest burden of the HIV pandemic.[1] These patients have absolute peripheral blood CD4 lymphocyte counts similar to those of Caucasian patients[2], but significant immunological discrepancies have been seen in patients of African origin.[3]

During the natural course of HIV infection, the CD4+ count decreases more slowly in patients of African origin than in Caucasian patients.[4] Previous studies have found the CD4+ count increase with highly active antiretroviral therapy (HAART) not to be significantly different between HIV-infected patients of African origin and HIV-infected Caucasian patients.[5] Only one investigation has reported evidence of a greater CD4+ count increase in Caucasian patients compared to patients of African origin during the first months of HAART.[6] Discrepancies between these studies could be linked to the low number of patients of African origin compared to the Caucasian patients, to the various geographic origins of patients of African origin, and to the time delay between the diagnosis of HIV infection and the initiation of HAART, as well as the potential impact of HIV-1 subtypes.[7]

The effect of ethnicity on the CD4 immune reconstitution during HAART remains an unsolved question, the answer to which could be of major interest. We conducted a retrospective epidemiological investigation to assess whether African ethnicity is independently associated with a poorer CD4 reconstitution during HAART.

2. Patients and methods

Five hundred and seventy-five HIV-1-infected adult patients under HAART on December 31, 2011, at the Reims University

☆ Data from this manuscript were presented at the 23rd European Congress of Clinical Microbiology and Infectious Diseases, Berlin, Germany, April 27–30, 2013, and the 14e Journées Nationales d'Infectiologie, Clermont-Ferrand, France, June 12–14, 2013.

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1201-9712/$36.00 – see front matter © 2013 Published by Elsevier Ltd on behalf of International Society for Infectious Diseases.
http://dx.doi.org/10.1016/j.ijid.2013.08.001

hospital center (France), who gave informed consent for the digitization of their medical records using Nadis software, were included.

Socio-demographic, clinical, and immuno-virological data (HIV-1 subtype, CD4+ count, and HIV-1 viral loads at baseline and during follow-up at 6, 9, 12, 18, 24, 36, and 48 months after beginning HAART) were extracted from Nadis. This database has been declared to the Commission Nationale Informatique et Liberté (number 1585477).

The baseline CD4+ count was defined as the lowest absolute value before HAART. Immunological success (IS) was defined as the presence of a CD4+ count >500 cells/mm^3 in more than 50% of the values collected during follow-up.[8]

Age, US Centers for Disease Control and Prevention (CDC) classification category B or C, and HIV-1 viral load at baseline were those extracted before the first line of HAART in patients with multiple lines of therapy. The last line was considered for immuno-virological data collection during follow-up, except when a previous line had lasted more than 48 months without any significant HIV-1 viral load variations (see exclusion criteria described below).

In accordance with the ANRS (Agence Nationale de Recherche sur le SIDA et les Hépatites Virales) algorithm,[9] HIV-1 subtype was defined as non-B in the presence of mutations at positions 35, 36, 61, 69, and 89 during routine *pol* gene sequencing.

The following patients were excluded: those displaying an HIV-1 viral load >20 copies/ml (TaqMan, Roche) 6 months after beginning HAART and those displaying an HIV-1 viral load >200 copies/ml, or more than one HIV-1 viral load between 20 and 200 copies/ml, from 9 to 48 months after beginning HAART. Patients lost to follow-up, with a duration of follow-up less than 9 months, and patients with a baseline CD4+ count >500 cells/mm^3 were also excluded.

2.1. Statistical analysis

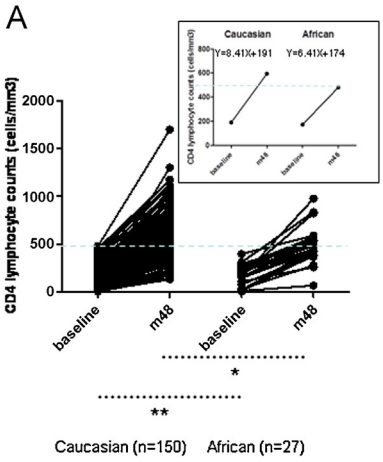
Quantitative variables were compared using the Mann–Whitney *U*-test and qualitative variables were compared using Fisher's exact test or Pearson's Chi-square test, as appropriate. A *p*-value of <0.05 was considered significant. All variables with a *p*-value of <0.20 were entered into a multiple logistic regression model. Statistical analyses were performed using StatView 5.0 software (SAS Institute, Cary, NC, USA).

3. Results

Two hundred and twenty (78.6%) Caucasian patients and 60 (21.4%) patients of African origin met the inclusion criteria and none of the exclusion criteria (Table 1). Study patients of African origin came mainly from West Africa (92%). Excluded patients were Caucasian in 80.7% of cases and patients of African origin in 19.3% of cases. HIV-1 viral loads decreased after initiation of first-line HAART in both groups (see **Supplementary Material**, Figure S1).

At 36 and 48 months after initiation of HAART, CD4+ counts were different between patients of African origin (n = 38 and 31) and Caucasian patients (n = 167 and 148): 469 (93–677) vs. 528 (45–1383) at 36 months (p = 0.03), and 449 (65–975) vs. 569 (131–1698) cells/mm^3 at 48 months (p = 0.02). CD4+ count reconstitution

A



B

Variables	No immunological success n=109 (100%)	Immunological success n=171 (100%)	MD	P*	Multivariate analysis OR	95% CI	P**
African origin (n=)	**31 (28.4%)**	**29 (16.9%)**	**0**	**0.02**	**2.22**	**[1.097 - 4.504]**	**0.02**
Age >50 years at the beginning of HAART (n=)	29 (26.6%)	35 (20.5%)	0	0.23			
Male sex (n=)	77 (70.6%)	112 (65.5%)	0	0.37			
Sexual transmission (n=)	96 (88.1%)	150 (87.7%)	15	0.27			
Chronic B or C viral hepatitis (n=)	15 (13.8%)	27 (15.8%)	0	0.64			
Median number of years since diagnosis of HIV-1 seropositivity (years) [min-max]	**10 [2-26]**	**12 [2-28]**	**0**	**0.04**	**0.96**	**[0.922 - 1.007]**	**0.09**
CDC Classification category B or C (n=)	**54 (49.5%)**	**67 (39.2%)**	**0**	**0.09**	**0.78**	**[0.408 - 1.485]**	**0.44**
Opportunistic infection (n=)	**55 (50.4%)**	**63 (36.8%)**	**0**	**0,02**			
Tuberculosis (n=)	3 (2.7%)	4(2.3%)	0	0,99[a]			
Median baseline blood CD4 cells counts absolute value (cells/mm3) [min-max]	**144 [1-338]**	**248 [1-479]**	**9**	**<0.0001**	**0.99**	**[0.988 - 0.994]**	**<0.0001**
Patients with HIV-1 viral load > 5 log10 (copies/ml) at baseline (n=)	39 (35,7%)	49 (28,6%)	19	0.38			
HAART regimen including Protease inhibitor (n=)	91 (83.4%)	137(80,1%)	0	0,47			
HIV-1 subtype non B (n=)	20 (18.3%)	18 (10.5%)	89	0.21			

Figure 1. (A) Blood CD4 lymphocyte count evolution at baseline and at 48 months (m48) after beginning HAART in HIV-1-infected Caucasian patients (Caucasian) and HIV-1-infected patients of African origin (African). *Median CD4 lymphocyte count absolute values at 48 months were 574 (range 131–1698) vs. 449 (range 65–975) cells/mm^3 in Caucasian and African patients, respectively (p = 0.02). **Median CD4 lymphocyte count absolute values at baseline were 188 (range 1–479) and 195 (range 4–396) cells/mm^3 in Caucasian and African patients, respectively (p = 0.63). Upper-right corner: mean CD4 lymphocyte count evolution at baseline and 48 months after beginning HAART in Caucasian and African patients. (B) Variables significantly associated with the absence of immunological success. Immunological success was defined as the presence of blood CD4 cell count absolute values >500 cells/mm^3 in more than 50% of the values collected during follow-up at 6, 9, 12, 18, 24, 36, and 48 months after beginning HAART. MD, missing data; OR, odds ratio; 95% CI, 95% confidence interval. *p-Value univariate analysis. **p-Value multivariate analysis. [a]Fisher's exact test. Hosmer and Lemeshow goodness-of-fit gives p = 0.163. 'HIV-1 subtype non-B' and 'opportunistic infection' were not included in the model because of collinearity with variables 'African origin' and 'CDC classification category B or C', respectively (Table 1).