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Full Length Research Paper

Determinants of non-immunological response with HIV infected patients on antiretroviral treatment in Centre Hospitalier Universitaire Souro SANOU, Bobo – Dioulasso (Burkina Faso)

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Objective: To study the determinants of non-immunological response with HIV infected patients on antiretroviral treatment in Centre Hospitalier Universitaire Souro SANOU (CHUSS), Bobo – Dioulasso. Methods: It was a historical cohort study from 2010 to 2014. We included all patients aged 1-18, infected with HIV and on antiretroviral (ARV) treatment followed at the pediatric day hospital and the Internal Medicine of CHUSS and non responders (INR) to ARV treatment. The INR was evaluated by the numeration of CD4 + cells on a flow cytometer (FACSCount V1.5). HIV patients were apportion according to the regimens received. (AZT + 3TC + NVP, AZT + 3TC + EFV; AZT + 3TC + LPV / r and AZT + ddI + EFV). A total of 351 children were followed clinically and biologically respectively in the pediatric departments of internal medicine and laboratory. The average age of patients was 12 years ± 5.6 with extremes from 1 to 18 years. The prevalence of immunological non-responders (INR) in our cohort was 9% (31/351) on antiretroviral treatment over an average period of 3.5 years. Of these, 3.41% were at WHO Stage C. Among the determinants to INR, males were found to be 5.98% (21/351) whose CD4 rate was 14%, type of ARV molecule, type of HIV. With 13% of INR, were prescribed AZT + 3TC + NVP regime. The average weight of the patients their age, and the average CD4 rate at treatment initiation were not found as determinants to INR. Conclusion: All the INR was HIV-1 and 13% were under AZT + 3TC + NVP regimen, the possibility of existence of stem CXCR4 is not excluded even if we had not been able to explore it due to financial constraints.

Keywords: Non immunological responders, HIV, antiretroviral treatment, Burkina Faso.

INTRODUCTION

AIDS is the ultimate stage of HIV infection. This virus has a tropism for CD4 T cells, the immune system is weakened after extensive destruction of these cells. Despite the introduction of new and highly effective antiretroviral treatments that significantly changed the prognosis of the disease, immunological non-responders (INR) still raise issues related to the scientific world especially with the determinants of the occurrence of these INR. Indeed, despite achieving undetectable viral load with patients remains the fact that CD4 do not rise. These dissociated immuno-virological responses could represent according to WHO about 25 to 30% of the treated population (ONUSIDA, 2010). Multiple deficits in the generation of

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T cells, excessive or persistent activation of the immune system attributed to HIV were raised to explain biologically the occurrence of this paradoxical response (Tambussi et al., 2010). In a resource limited context thymic exploration remains a constraint, however the study of some socio-demographic, clinical and therapeutic factors associated with these dissociated responses would allow to better understand the context in which this INR occurs. Thus the objective of this work was to study the determinants of non-immunological response with HIV infected patients on antiretroviral treatment in CHUSS.

PATIENTS AND METHODS

It was a historical cohort study from 2010 to 2014. The recruitment and the clinical follow up of our patients were performed in the pediatric department of internal medicine of the Centre Hospitalier Universitaire Sourô Sanou (CHUSS). The lymphocyte count was Conducted in the laboratory department of Immunology and Hematology of CHUSS. The target population consisted of both patients infected with HIV-1 and HIV-2 (Burgard, 2005; Bürgisser et al., 2000). Were included subjects aged 1-18 on antiretroviral therapy (ART) and identified as non-immunological responders during the follow-up period, i.e. having a CD4 rate which has not risen. The gain of CD4 T cells should be greater than 150 cells / mm³ after 12 months of antiretroviral therapy to be an immunological success. With all INR the CD4 rate was below 100 cells / mm³, six months after initiation of ARVs and throughout all the follow-up period, in others a return to pre therapeutic initial rate was observed in the lack of any opportunistic infection. For under-age the consent of the parents or legal guardians was obtained before inclusion. HIV patients were apportion according to the regimens received. (AZT + 3TC + NVP, AZT + 3TC + EFV; AZT + 3TC + LPV / r and AZT + ddI + EFV). The sample size was calculated using the formula: $N = (Z\alpha / 2)^2 pq / I2$ $(Z\alpha / 2) = 1.96$, $P = Q = 30\%$ 70% $I = 5\%$. $N = 3.8416 \times 30 \times 70/25 \cong 323$ *subjects*. So we selected a sample of 351 children infected with HIV and the choice was made randomly. The Following variables were selected as influencing the non-immunological response (INR) with infected subjects on ARVs.

Socio-demographic characteristics: age, sex. Clinic: weight, WHO staging. Therapeutic: the kind of regimen, setting ARV treatment duration.

Biological: HIV type, CD4 count, viral load.

Biological analyzes

It was about taking a sample of 2-4ml venous blood at the elbow bent using a dry tube with anticoagulant (EDTA) for the diagnosis of HIV and CD4 count in relative value respectively. The samples were labeled after sampling then centrifuged at 3000 rpm for 5 minutes. The serum obtained was used to make the diagnosis of HIV-1. We used an immunochromatographic test (Determine®) for detecting anti-HIV-1 antibody - 2 in the serum - and an ELISA test (ImmunoComb®II) for confirmation of our results and serotyping. The dosage of CD4 was performed by flow cytometry (FACSCount ® v 1.5).

Statistical analysis

Each time, the average CD4 rate was calculated. The data were entered using the Word 2007 software and statistical processing and graphics were performed using Excel and Epi Info software V 15.2. The chi-test and two Fisher exact tests were used for comparison of means and proportions. The test was significant if $p < 0.05$.

Ethical aspects

confidentiality was respected and the data were also confidential. This study has obtained the approval of the National Ethics Board of Burkina Faso.

Demographics of patients

In total of 351 patients were followed clinically and biologically respectively in the pediatric department, the internal medicine and laboratories. The age of patients was 12 years ± 5.6 with extremes of 1 to 18 years. The prevalence of immunological non-responders (INR) in our cohort was 9% (31/351) on antiretroviral treatment over an average period of 3 ½ years. Of these, 3.41% were at WHO Stage C. The prevalence of male subjects and that of female subjects non-immunological responders was respectively 5.98% (21/351) and 2.94% (10/351).

RESULTS

Distribution of the average rate of CD4 INR based on the average weight

At the initiation of treatment the average CD4 rate was 17.2% with patients between 21 and 42 kg. It was 20% with patients between 43 and 64 kg and 16, 1% with patients less than 21 kg. No statistical relationship was associated with the average CD4 rate at treatment initiation, the weight and the occurrence of INR *(P = 0.07)*.

Distribution of the average rate of INR CD4 depending on the type of antiretroviral

With INRs, the increase of the average CD4 rate was significantly greater with infected subjects who received the combination: zidovudine (AZT) + lamivudine (3TC) + efavirenz (EFV); AZT + 3TC + lopinavir / ritonavir (LPV / r) and AZT + (didanosine) ddI + EFV than on AZT + 3TC + NVP ($P = 0.04$).

Figure 1 shows the distribution of the average CD4 rate of immunologic non-responders based on the antiretroviral type.

Distribution of immunological non-responders according to the type of HIV

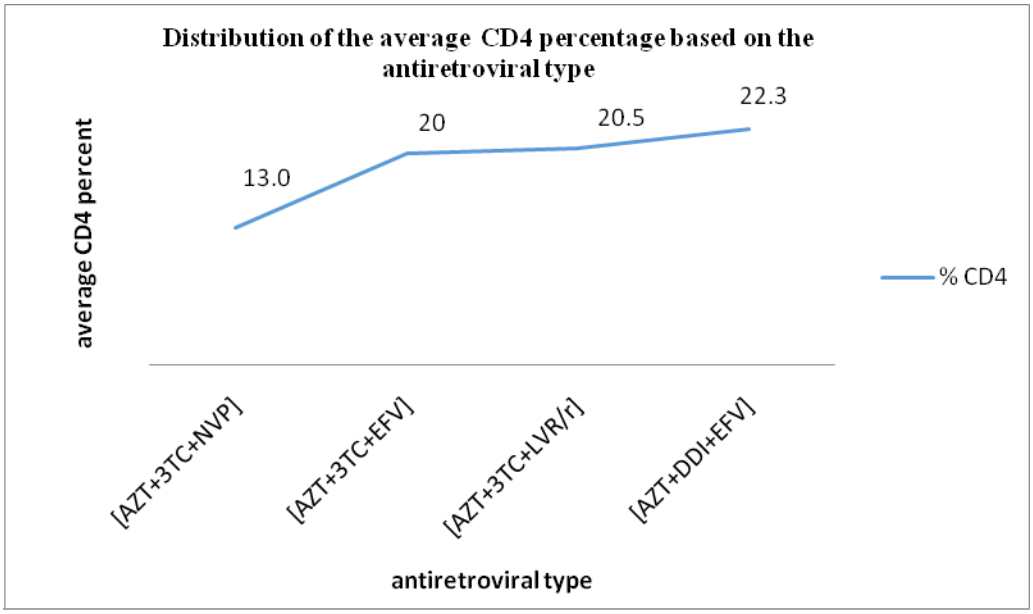

Figure 1. Distribution of average CD4 rate depending on the ARV regimen prescribed to immunological non-responders.

All cases of INR were those infected with HIV-1.

Distribution of the immunological non-responders average CD4 rate per gender.

With INRs, the average CD4 rate was significantly higher with infected female subjects (19/31) than with infected males (14/31) (p = 0.012).

Distribution of immunological non- responders average CD4 rate according to age

The lower value of CD4 was noticed with infected INR subjects who were more than 16. Figure 2 shows the distribution of the immunological non-responders average CD4 rate according to age.

DISCUSSION

Prevalence of immunological non-responders

The prevalence of INRs over an average of 3.5 years of follow-up and on ART was 9% (31/351). Very few studies have been conducted with children to determine the prevalence of immunological non-responders.

But by comparing our results with those obtained with adults, this rate is lower than that reported by Michon in France which is 17% (Michon Christophe,2003) and Jlizi in Tunisia which was 42.22% of non-immunological responders (Jlizi et al., 2009).

Although we cannot deny the involvement of genetic susceptibility, early detection of subjects in our study with early initiation of ARV treatment associated with less use of nevirapine and good treatment adherence in our cohort are as assumptions that may explain the noticed differences.

Distribution of immunological non-responders by gender

The prevalence of infected male and female non-immunological responders in our study was 5.98% and 2.94% respectively. Our results, which are shared by Bashi through a multicenter study in five countries (Benin, Ivory Coast, Senegal, Gambia, Mali) reported a predominance of INR among males 60% vs 40% with female subjects (Bashi et al., 2010) as well as Mouhari-Touré who had found an INR rate of 68.6% with male patients (Mouhari-Touré et al. 2011). Although the pathophysiological mechanism remains unsolved up to this day, some authors relate rapid immune reconstitution to males (Bashi et al., 2010;Mouhari-Toure et al., 2011).

Distribution of the average CD4 rate according to the type of antiretroviral

The average CD4 rate with INRs was relatively lower in the regimen containing NVP (AZT + 3TC + NVP) 13% than in the therapeutic diets that did not contain NVP or rates of over 20% (AZT + 3TC + EFV; AZT + 3TC + LPV / r and AZT + ddI + EFV). The same observation was made by Catherine in Southern Africa (Catherine Seyler, 2008).

The resistances noticed with NVP (nearly 90% with children) could explain the lower average CD4 rate with INRs whose regimen contained this molecule (Nicolas et al., 2010; Chaplain et al., 2006).

Distribution of the average CD4 rate according to age

With INRs, the average CD4 rate over an average of 3.5 years of follow-up and on ART varied according to age, it was low (8.32%) with subjects between 16 and 18.

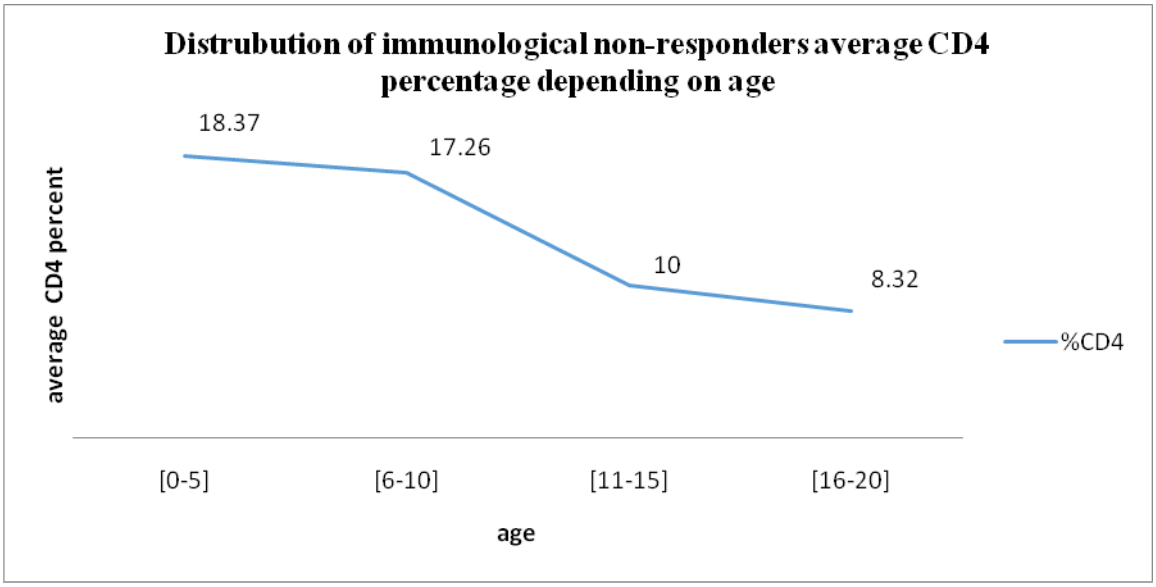

Figure 2. Distribution of the average value of the immunological non-responders CD4 rate according to age.

It is accepted by most authors that the number of CD4 T-cell gradually decreases from the first year of life to reach values close to those noticed with young adults from the age of 5 years in normal state **(**Ekpini et al., 2005; Francesca et al., 2010).

CONCLUSION

The prevalence of non-immunological responders (INR) was 9%.This prevalence appears to be satisfactory in comparison with the prevalence expected in most countries according to WHO. The prevalence of WHO varies between 25 and 30%. Determinants associated with INR were male with a CD4 rate of (14%), treatment regimens including NVP, the type of HIV; but the possibility of existence of stem CXCR4 is not denied.

Conflict of interest:

Authors declared no conflict of interest opposing them.

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