Knowledge and adherence to antiretroviral therapy among adult people living with HIV disease followed-up in the health care centers of the “Espoir Vie Togo” association, in Togo, west Africa

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Abstract

Background: The efficacy of antiretroviral therapy (ART) which depends on a near perfect level of patients’ adherence is few documented in our context. The aim of the present study
was to examine the knowledge, the adherence level and associated factors to antiretroviral therapy (ART) among HIV-infected patients followed-up in the HIV/AIDS health care centres of “Espoir Vie Togo” association, in Togo, west Africa.

**Methods:** We conducted a prospective survey among adults people living with HIV/AIDS (PLWHA) through a structured questionnaire.

**Results:** A total of 99 patients were enrolled. Among them, 55.6% knew the name of antiretroviral agents of regimens prescribed. All patients had a good knowledge of treatment schedule. The treatment regimens based on 2 NRTIs + 1 NNRTI were used in 90% of patients. The mean monthly adherence rate was 89.8% while 62.62% of patients exhibited adherence rate of 95% or greater. The treated groups were similar in term of % median of non-adherence rate according to PLWHA characteristics. The factors associated with the poor adherence were forgetting (34.5%), travel (25.6%), cost of treatment (13.9%) and side effects (11.6%).

**Conclusion:** These results should encourage the association and all actors in the HIV/AIDS’s program to strengthen counselling, education and information interventions for HIV-infected patients in order to overcome the potential barriers of poor adherence.

**Key words:** Antiretroviral therapy; adult people living with HIV/AIDS; adherence; poor adherence factors; “Espoir Vie Togo” association.

**Background**

Since 1996, progress in the field of antiretroviral therapy have resulted in the reduction of nearly 80% of deaths, the number of cases of acquired immunodeficiency syndrome (AIDS) and the incidence of opportunistic infections [1]. About twenty drugs belonging to 4 classes defined according to their pharmacological modes of action is the current arsenal of antiretroviral drugs (ARVs). The combinations of these drugs have dramatically changed the
prognosis of an infection which natural history was lethal in more than 90% of the patients in chronic infection [2,3]. The long-term nature of the disease has more complicated its management. In this context, sustained adherence is an essential tool of the long-term effectiveness of ARVs therapy [4] (e.g. significant reduction in viral load, drug resistance, deterioration of health status and treatment failure) [5-8]. In addition, the role of knowledge of treatment regimens [9] and cognitive demands related to the complexity of ARVs pharmacotherapy [10,11] were reported as factors that may influence the level of adherence[12,13]. Recent studies on patients’ adherence in African health contexts showed that it is relatively higher than that of industrialized countries health context [14,15].

Cohorts followed in developed countries have emphasized the frequency of non-adherence situations and the high level of adherence required to obtain optimal effectiveness of ARVs chemotherapy, delay the onset of human immunodeficiency virus (HIV) resistance and pejorative evolution of the disease [16].

The assessment of adherence, parameter that has no standard method of measurement, which varies over time, meets a number of methodological difficulties [5]. Few studies have documented the factors involved and the level of adherence of adults people living with HIV/AIDS (PLWHA) to ARVs therapy in Togo, West Africa. The objectives of the present study were to assess the knowledge of the treatment regimens prescribed to patients; quantify the level of adherence to ARVs therapy and to identify the factors related to non-adherence.

**Eligible patients and method**

This was a prospective study carried out during the months of August and October 2005 in the HIV/AIDS health care centers (in urban areas of Lomé and Sokodé) of the association “Espoir Vie Togo” (EVT), the first organized non-governmental organization including people living with HIV/AIDS and those contributing to their support. The association is accredited by “Programme National de Lutte contre le SIDA” (PNLS-Togo) as an ambulatory HIV/AIDS
health care association. The association also deals with ARVs purchasing for the members of the association from “Central d’Achat de Médicaments Essentiels sous nom Générique” (CAMEG-Togo). The ARVs delivery to patients, takes place in EVT’s pharmaceutical stores. We interviewed eligible HIV-infected adults when they came to EVT’s pharmaceutical stores to get their monthly allocation of ARVs. The enrolment was done on a voluntary basis.

**Inclusion criteria**

To be enrolled in the study, HIV-infected patients met the following criteria: all adult patients over 15 years, members of EVT association, placed on ARVs therapy for over 1 month, receiving ARVs in EVT pharmaceutical stores. Hospitalised patients and those whose age is below 15 years were excluded from the study.

**Data collection method and variable of interest**

A cross-sectional survey was conducted from a structured questionnaire submitted to enrolled patients (face-to-face interviews for about 30-45 mn). The data of interest were collected for a period covering one month (August to October 2005). Data collected concerned the following variables:

- The characteristics of patients (sex, age, educational level) and ARVs procurement;
- The patient treatment knowledge which was assessed on the getting control or not of names of different drugs prescribed, their respective dosages (number of tablets per dose and number of daily intakes) and the times of intake. The statements of patients were compared with the prescriptions and the treatment regimens mentioned in their health card;
- The type of ARVs combination regimens prescribed;
- The rate of adherence to treatment. It was evaluated in the last month and defined as the number of doses taken during the last 7 days before each interview. Adherence score was expressed as the proportion (%) of tablets taken to prescribed tablets. An adherence rate of 95% was considered to be good.
- The factors that induced poor adherence to treatment.

As the Ethic Committee was not available at the period of the study, the Ministry of the Health authorised the survey.

Statistical analyses
The % median of non-adherence rate of treated groups were compared using ANOVA method (Sigma Stat32 software; Jandal Corp, San Rafael, CA): Mann-Whitney Rank sum test was used to compare treated groups according the sex, the ARVs procurement and the ARVs combination used; Kruskal–Wallis one-way analysis of variance on ranks method was used to compare treated groups according the age groups and the educational level. The difference between the groups was considered to be significant if P < 0.05.

Results
A total of 99 patients (77.3%) of 128 interviewed during the investigation, accepted to be submitted to the questionnaire.

Sex and age of patients
Of the total sample (n = 99), 76 were female (76.8%) vs. 23 male (23.2%) with a sex ratio of 0.3. The age of patients range 21-57 years, with an average age of 36.8 years. The age group from 36 to 45 years was more representative (39.4%) followed by 26 to 35 years (34.3%).

ARVs procurement
All the patients in this study were supported for receiving ARVs: Sixty one percent were under an individual financial participation of “5 000 fcfa” per month (approximately US $ 11 reduced to US $ 2 since November 2005), the remaining received ARVs free of charge.

Treatment regimen knowledge
Forty four patients (44.4%), knew perfectly the names of various ARVs included in the combination regimens. All respondents had a perfect knowledge of the treatment schedule (number of tablets per dose, the number of daily intakes and the times of drug intake).

**Types of ARVs combinations prescribed**

All patients have received a combination of three ARVs. Four different ARVs combinations (ARVs-GF (Global Fund)) were legalized, of which one available fixed-dose combination (lamivudine + stavudine + nevirapine). Only 39.4% of patients have received this fixed-dose combination vs. 60.6% who were placed on non-fixed-dose combinations.

The treatment regimen containing 2 nucleoside reverse transcriptase inhibitors (NRTIs) + 1 non-nucleoside reverse transcriptase inhibitor (NNRTIs) was used in 89.9% of patients; While the remaining 10.1% were placed on 2 NRTIs + 1 protease inhibitor (PI) based regimens (Figure 1).

**Adherence rate to ARVs therapy**

The mean monthly adherence rate was 89.8% while sixty two (62) patients (62.62%) reported the monthly doses intake of 95% or greater. Table 1 shows the repartition of non-adherence rate (% and % median) according PLWHA characteristics. Except patients group who received 2 NRTIs + PI combination (46% median non-adherence rate), the % median rate of non-adherence varies from 82% to 92%.

**Factors of non-adherence**

Forgetting (34.9%), travel (25.6%), the cost of treatment (13.9%) and side effects (11.6%) were the main factors of poor adherence reported by the 43 patients who missed at least once a dose intake (Figure 2). They reported using a method to not forget the medication intake. Among them 69.4% stated using a watch and/or an alarm clock to remember the time of drug intake. In 27.9% of cases, parents would remind patients of the medication intake.
Twelve patients (12.1%) stopped or changed one or more ARVs included in the treatment regimens because of side effects in 6 patients (6.1%), ineffectiveness in 4 patients (4%) and because of disease in 2 patients (2%).

**Discussion**

The assessment of the adherence rate by interviewing PLWHA, seems an appropriate method in Africa. It is simple, inexpensive and accessible. This method has, however some limits (the length of interview, the subjectivity of patient statements). The fact that the investigator is unknown by patients, that he is not member of health care team and the guarantee of patient’s anonymity limit this bias (e.g. the patient did not have fear of remonstrance for poor adherence). Adding to this method a more objective (e.g. a count of returned pills) would have helped to improve the estimation of adherence level.

The sex ratio in the present study (0.3 with 76.8% of women) is twice as high compared to that observed by PNLS [17] and lower than that of South Africa (0,4) [18], Uganda (0,5) [19] and Senegal (1) [20] cohorts. Previous reports in Senegal [21], Morocco [22] and Benin [23] have observed a highest proportion of male. The age of patients in our study ranged from 21 to 57 years, with an average of 36.8 years. This age average is similar to that of PNLS [17] but less than that reported in Senegal (38 years) [20] and higher than that observed in Kenya (31.5 years) [24], Morocco (35.5 years) [22] and in Bothswana (35.6 years) [25].

The whole eligible patients followed the regimens and the treatment schedule prescribed compared to Diabate et al’s report in Ivory Cost (76.2% of the patients followed their regimen special instructions vs. 63.6% who took their medication at the prescribed time) [26]. However, only 55.6% (n = 55) knew perfectly the names of ARVs prescribed. This proportion can be explained by the high proportion of illiterate patients (19.2%). As previously reported, treatment knowledge [9] and the cognitive demands related to complexity of ARVs pharmacotherapy [10,11] have been targeted as necessary components of adherence.
Standard triple-ARVs combination regimens were prescribed. Four types of ARVs combinations of which two were based on 2 NRTIs + 1INNTI (standard first-line regimen proposed by WHO) and two on 2 NRTIs + 1 IP (Figure 1) were used vs. 16 different combinations reported by Roux et al [23] in Benin.

Nearly 90% (n = 89) of patients were in 2 NRTIs + 1INNTI-based regimens (Fig. 1). This proportion is similar to that observed by PNLS-Togo (90.8%) in a national evaluation of ARVs therapy [17] Two NRTIs + 1NNRTI-based regimens available in many other sub-Saharan African countries [18-20,25,26] are recommended because of their virologically and immunologically efficacy. These regimens contribute to improve adherence as there is an available fixed-dose combination (lamuvidine + stavudine + nevirapine) as first-line ARVs regimen. This fixed-dose combination available in other African countries [19,26] used by 39.4% (n = 39) of patients was highly appreciated because it requires only 2 daily intakes of one tablet, promoting adherence.

The mean monthly adherence rate was 89.8% of the doses prescribed. It is close to that observed in Senegal (91%) [21,20], but lower than that reported by Vriesendorp et al [25] in Botswana (98%) on the basis of patients’ reports. Sixty two patients (62.62%) exhibited adherence rate of 95% or greater vs. 56% having taken 100% of the doses of medication; indeed, several studies showed that 90% to 95% of medication doses should be taken for optimal virologic suppression and reduction of virologic failure[27] but according to two studies, a moderate adherence (80-90%) should lead to better viral suppression under more potent regimen including NNRTI [28,29]. Otherwise, adherence rate of 95% or greater is strongly correlated with CD4 cell count increase, viral load and morbidity decreases [6]. This proportion of 62.62% is less than previous reports in Ivory Cost (74.3%) [26] and in Senegal
(78%) [20] with adherence score of 95% or greater. Adherence level could be improved if adherence data sheets updated by prescribers were available allowing patients follow-up.

Table 1 includes the % rate and % median rate of non-adherence according to patients characteristics. No significant difference have been observed between the treated groups according the characteristics such as the sex, the age groups, the educational level, the ARVs regimen received and the ARVs procurement (p >0.05). Ours findings confirm those of previous studies [19,30] concerning the sex, the age groups (excluding younger age) and the educational level. This lack of difference in treated groups could be explained by the PLWHA consciousness rising on the role of ARVs therapy adherence by the ‘‘Espoir Vie Togo’’ association.

The existence of tools or methods to promote the adherence is also available. In the present study, 43.4% (n = 43) of patients reported using at least one (69.4% reported using a watch / alarm clock to remember the times of medication intake) compared to 27.9% who stated being reminded by parents.

Forgetting (34.5%, n = 15), travel (25.6%, n = 11), the cost of treatment (13.9%, n = 6) and side effects (11.6% n = 5) (Fig. 2) have been cited by 43 patients having missed at least one dose of treatment as the main factors influencing the adherence score and often reported in similar studies [15,19,24].

Missing drug intake is mainly related to well being feeling experienced by the patients, lack of the 3 daily meals (specific factor in Africa) [31-33] of which the medication intake is regulated and a feeling of weariness suitable for all long-term treatment. It is therefore a need to strengthen advice and information on the evils of poor adherence for the patient himself and the threat for the public health when he does not take his medications.

Travels were the second main factor of poor adherence. This factor of non-adherence reveals the problem of the lack of a pill container containing at least all daily doses.
The cost of treatment comprising transport, food support and laboratory tests were cited as main obstacles to optimal adherence. Previous studies have reported the incidence of payment factor on the rate of loss in HIV-infected patients follow-up and/or adherence in Kenya [24]. The risk of reduction in terms of loss to follow-up related to offering ARVs free of charge was 56.6% in cohorts study [24].

Side effects were the 4th barrier of non adherence (11.6%). They were collected on the basis of patients’ reports. As a result, we have not considered appropriate to mention them since not validated as such in contrast to the report of Bhengu et al [34] who conducted a study on the prevalence of symptoms reported by patients. They have been also reported (including their severity) as main factors for poor adherence in previous studies [9,25,35,36]. On the contrary, Bhengu et al [34] observed no significant relationships between adherence and the intensity of symptoms. Of the 99 patients in this study 89 patients (89.9%) reported side effects due to ARVs treatment received. This proportion is higher than that reported in a national survey by PNLS (31.6% of PLWHA) [17]. In this study, five patients (11.6%, n = 43) failed to take their medication because of side effects. The influence of these side effects may be lessened by a good patient information and training to enable them to manage himself some minor effects.

A total of 12 patients (12.1%) stopped or changed one or more ARVs of the combination regimen (6.1% for side effects, 4.0% for ineffectiveness of treatment and 2.0% for illness conditions) compared to 49.9% reported in the national survey conducted by PNLS [17].

Overall, a review of the literature shows that the ART-adherence determinants include institutional, socio-economical, psychological and therapeutic factors to take in account in the management of PLWHA care. Our findings suggest the improvement of PLWHA follow-up by the help of adherence data sheets, the counselling/information/education interventions

10
concerning the virological, biological, therapeutic and public health risks of non-adherence to ARVs therapy.

Conclusion and recommendations
Our results have shown that the knowledge and the capacity for adherence to ARVs treatment of PLWHA in the present study are satisfactory but have not reached the optimum level desirable. However, these results reflect the quality of the "Espoir Vie Togo" association interventions toward PLWHA. They should encourage the association EVT and all actors in the fight against AIDS to maintain and strengthen counselling, education, training and information interventions for PLWHA with a view to overcome the potential barriers of poor adherence as non-adherence leading to the development of ARVs-resistant HIV is a public health concern.

Abbreviations

Competing interests
The authors declare that they have no financial or no non-financial competing interests in relation to the present manuscript.
Authors’ contributions
YP conceived, designed and coordinated the study, he carried out statistical analysis and drafted the manuscript; KT participated in the design of the study and the questionnaire, he carried out the study (interviewing and data collection), used the data collected for sustaining a doctor thesis of pharmacy ; AB, VPP and IPG contributed by means of their respective competence and their experiences to the manuscript reviewing. All authors read and approved de final version of the manuscript.

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References


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Figure 1. Distribution of patients according to ARVs combination regimens prescribed

(a) : 3TC+D4T+NVP ; (b) : AZT+3TC+EFV ; (c) : ddi+D4T+IDV ; (d) : ddi+D4T+NFV

AZT = zidovudine ; 3TC = lamivudine ; EFV = efavirenz ; D4T = stavudine ;
NVP = nevirapine ; ddi = didanosine ; IDV = indinavir ; NFV = nelfinavir
Figure 2. Distribution of patients (n = 43) according to factors of poor adherence

Table 1. Repartition of rate and median rate of non-adherence according to PLWHA characteristics
<table>
<thead>
<tr>
<th>Epidemiological Characteristics</th>
<th>Rate of non-adherence (&lt; 95%)</th>
<th>% median rate of non-adherence</th>
<th>P value</th>
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<td>2 NRTIs + 1 NNRTI</td>
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<tr>
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NS : no significant
(a) : 3TC+D4T+NVP ; (b) : AZT+3TC+EFV ; (c) : ddi+D4T+IDV ; (d) : ddi+D4T+NFV

AZT = zidovudine ; 3TC = lamivudine ; EFV = efavirenz ; D4T = stavudine ;
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Figure 2 Distribution of patients according to ARVs combination regimens prescribed
Figure 2. Distribution of patients (n = 43) according to the factors of poor adherence
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