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Monitoring of HIV-Infected Children Receiving Highly Active Antiretroviral Therapy in Togo: A Multicentric Study of 854 Children

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Abstract

Objective: The purpose of this study was to document the outcome of HIV-infected children receiving the Highly Active Antiretroviral Therapy (HAART) in Togo.

Patients and method: It was a retrospective and descriptive multicentric national survey based on records of HIV-infected children who started receiving the HAART before the 31st of June 2010. The study was conducted in 14 sites throughout the country.

Results: 854 children (under 15 years old) out of 1257 monitored in Togo were included in the survey. During the study period, 715 (84%) of those children were stable patients, always watched over at selected sites. To be noted also, 56 deaths (6%), 69 follow-up lost (8%) and 14 transfers to other sites (2%). Death and follow-up losses rates were higher in children under one year with respective percentages 11.9% and 18.6%. The rate of death was 13.7% in the cohort of 2007, 10.8% in the cohort of 2008, 6.5% in the cohort of 2009 and finally 5% in the cohort of 2010. The survival rate at 12 months was greater than 90% in all the cohorts.

Conclusion: This study shows a gradual improvement in the survival rate of HIV-infected children receiving the HAAART from 2007 to nowadays. The survival rate of children receiving the HAART at 12 months is not different from that of adults. So, it is important to improve qualitative and quantitative care of HIV-infected children in public health programs in sub-Saharan Africa.

Keywords: Child; HIV infection; Loss to follow up; Survival; HAART

Introduction

The best strategies to prevent mortality and morbidity of HIV infection in children are not only the Prevention of Mother-to-Child HIV Transmission (PMTCT) programs expenditure, but also the availability of early diagnosis and antiretroviral therapy in a timely manner [1-4]. In this context, World Health Organization (WHO) in 2010 has published the update of guidelines on antiretroviral therapy criteria in children [5]. These criteria have an emphasis on early antiretroviral therapy in HIV-infected children in order to reduce the morbidity and mortality in this age group. According to the UNAIDS report in 2010, sub-Saharan Africa alone accounts for 92% of pediatric HIV infections and 80% of deaths in HIV-infected children [6]. In 2009, the prevalence of HIV infection in Togo was 3.2% in the general population, and out of the 120,000 people living with HIV (PLWHA), 10% were children [7].

In Togo, the implementation of mother-child pair interventions started since 2004 (the PMTCT, the free of charge availability of antiretroviral drugs and laboratory tests, the multiplication of antiretroviral drugs delivery locations, the fixed dose combinations of pediatric formulations) has improved gradually pediatric care with an increase in the number of children receiving the HAART, which increased from 607 in 2008 to 1357 at the end of 2010 [8]. Data on mortality and morbidity of HIV-infected children in sub-Saharan Africa is relatively less important when compared to data in adults [9-14,15]. In Togo, in order to evaluate the interventions of the National AIDS Program that will help in strategic information for improved planning, it was essential to provide the outcome of pediatric care in PLWHA treatment centers. This study specifically aimed to inform on the rates of mortality, follow-up losses of HIV-infected children receiving the HAART in Togo's health program.

Patients and Method

It was a retrospective multicentric national survey based on records of HIV-infected children who started receiving the HAART before the 31st of June 2010. The study was conducted in medical management of PLWHA sites throughout the country. A number of 14 sites were selected according to the following criteria: i) the prescription of antiretroviral drugs in the site started more than five years ago; ii) the availability of a pediatric unit in the site (Table 1). All the HIV-infected patients (under

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Health regions subdivisions	Sites	Type of care center	Number of children included.
Lom e-Commune	Teaching hospital of Tokoin (pediatrics)	Public	186 (21.8%)
	Regional hospital of Lome commune	Public	20 (2.3%)
	Bè hospital	Public	66 (7.7%)
	EVT Lome	Associative	101 (11.8%)
	AMC Lome	Associative	94 (11%)
Maritime	Disctrict hospital of Kouve	Confessional	120 (14.1%)
	Regional hospital of Ts evie	Public	31 (3.6%)
Plateaux	Regional hospital of Kpalime	Public	23 (2.7%)
	Regional hospital of Atakpame	Public	31 (3.6%)
Centrale	Regional hospital of Sokode (AED LIDAW)	Public	86 (10.1%)
	EVT Sokode	Associative	26 (3%)
	District hospital of Koloware	Confessional	24 (2.8%)
Kara	Teaching hospital of Kara	Public	26 (3%)
Savanes	Association « Vivre dans l'esperance »	Confessional	20 (2.3%)
Total			854 (100%)

Notes: EVT : Espoir Vie Togo ; AMC : Aide Medicale et Charite ;

Table 1: List of sites selected by health regions and sectors.

15 years old) at the time of the HAART initiation were included in the study. For each child, a questionnaire was used to collect demographic data (age and gender), clinical data (testing conditions and WHO stage), laboratory data (type of HIV and number of T4 lymphocytes), therapeutic data (antiretroviral therapy) and outcome information (lost to follow-up, death or transfer). It had been considered that a child receiving the HAART was lost to follow-up when he was not seen for more than six months in the care center. During the study, the HAART initiation criteria and the regimens were those of WHO in 2006 [16] (Togo has begun the implementation of WHO 2009 recommendations only in April 2011). Moreover, viral load was not available and early diagnosis by Polymerase Chain Reaction (PCR) in children started only in July 2009. Data were collected from patient's records using ESOPE software (Operational Evaluation and Monitoring of active files of PLWHA: software developed by the program ESTHER). These data were validated in a sample of 10 sites that were randomly selected. The validation consisted of verifying that all the data extracted through ESOPE software in the sites were identified.

Results

During the study, from the 1,257 children who started receiving the HAART in June 2010 in Togo, 854 (67.9%) were included in our survey (Table 1). The 854 children were divided into four cohorts according to the year of the HAART initiation. The children put on the HAART from 1998 to 2006 were gathered in the 2007 cohort because of their small number (Table 2). In view of the number of children and duration of follow-up (at least 12 months), we analyzed the survival of only three cohorts (2007, 2008 and 2009). The average age of these children at the HAART initiation was 5±3 years (extremes: 3 months and 14 years). The HAART initiation criteria were observed in 92.7% and the HAART initiation regimens were in accordance with national guidelines in 96.8% of cases. At the time of data collect, 715 (84%) children were always watched over at selected sites. There had been 56 deaths (6%), 69 children were lost to follow-up (8%) and 14 children were transferred (2%) to other sites. By comparing the different cohorts, it was remarked that the death rate was going down in recent cohorts, with 13.7% in the 2007 cohort, 10.8% in the 2008 one, 6.5% in the 2009 cohort, and finally 5 % in the 2010 cohort. The one-year survival rate was 90.8% for the 2007 cohort, 91.8% for the 2008 one and 96.2% for the 2009 cohort. A 2-year survival rate was 89.1% for the 2007 cohort and 90.1% for the 2008 one. And 3-year survival rate was 85.4% for the 2007 cohort.

Discussion

This study has led to the description of the outcome of more than two thirds (67.9%) of HIV-infected children under HAART in Togo in 2010. Death and losses to follow-up rates were respectively about 6% and 8%. This death rate is lower than the death rate found in the study of the Working Group IeDEA (9.6 deaths per 100 child-years) in children on HAART in West Africa [15]. Although the death rates declined steadily since 2007, probably because of progress made in pediatric care in Togo, they were probably underestimated, if it must be taken into account the children who were lost to follow-up (because the outcome of those children is unknown). Indeed, according to Braitstein et al. [17] in Kenya, 16% of HIV-infected children who were lost to follow-up had died. The study found that mortality was the second cause of losses to follow-up of children after the concealment of HIV status by parents for fear of discrimination. Similarly in Malawi, McGuire et al. [18] had assessed the outcome of HIV-infected patients who had missed one appointment for medical care for more than one month, and their results show that 50% of children who missed their appointments had died. Other causes of children losses to follow-up are travelling, unaffordable transport cost, family conflicts, traditional treatments, dissatisfaction with health care professionals, apparent improvement in child health [17,18]. The prevention of children losses to follow-up must be understood at two levels: the primary prevention which is to intensify the fight against discrimination and stigma, multiply and create network between HIV management centers, improve quality services in these centers; the secondary prevention will focus on active and early research of the loss to follow-up patients by telephone calls and or home visits.

A significant reduction in mortality and morbidity is known since the advent of antiretroviral therapy in 1996 in Europe [19]. This reduction is less pronounced in sub-Saharan Africa because of the delay in starting treatment due to the low coverage of PMTCT services and screening services. In this study, mortality was higher in children under one year (11.9%). This is in accordance with previous studies [20], especially in Africa where a multicenter study had found that the risk of death during the first and second year of life among HIV-infected children were respectively of 35.2 % and 52.5% [21]. In this study, the maternal death, the immune level of the mother, and the early HIV infection (before the first 4 weeks of life) were factors significantly associated with early death of children during the first 2 years.

Sex (N=849)	Male	442 (52%)
	Female	407 (48%)
	Sex-ratio (male/female)	1,1
Age group (N=854)	[0-1]	149 (17%)
	[1-5]	257 (30%)
	[5-10]	352 (41%)
	[10-14]	96 (11%)
Average time of monitoring	20 ± 30 month	
Circonstances of screening (N=321)	PMTCT	112 (35%)
	Clinical suspicion	175 (55%)
	Volontary test*	34 (11%)
Type of HIV (N=623)	HIV_1	621(99.7%)
	HIV_2	0 (0%)
	HIV_{1+2}	2 (0.3%)
WHO clinical stages (N=517)	Stage 1	149 (29%)
	Stage 2	112 (22%)
	Stage 3	184 (36%)
	Stage 4	72 (14%)
T4 lymphocytes number (N=624)	Average for children 0-5 years	635±528
	Average for children over 5 years	312±275
Therapeutic regimens (N=854)	D4T 3TC NVP	528(61.8%)
	AZT 3TC NVP	251(29.4%)
	AZT 3TC EFV	25 (2.9%)
	AZT 3TC ABC	2 (0.2%)
	ABC DDI LPV/r	21 (2.5%)
	ABC 3TC LPV/r	1 (0.1%)
	AZT 3TC LPV/r	22 (2.6%)
	TDF 3TC LPV/r	4 (0.5%)
Repartition of children in cohorts	2007 cohort	103(12.1%)
	2008 cohort	68 (8%)
	2009 cohort	219(25.6%)
	2010 cohort	293(34.3%)
	Unknown HAART initiation date	171 (20%)

N : number of disponible data; PMTCT : mother-to-child HIV transmission; D4T : stavudine; 3TC : lamivudine; NVP : nevirapine; ABC : abacavir; AZT : zidovudine; DDI : didanosine; TDF : tenofovir; EFV : efavirenz; LPV/r : lopinavir/ritonavir; * Testing on request of parents or gardians

Table 2: Characteristics of children included.

In the study of the Working Group IeDEA, only 2% of children had started HAART before the age of one year, however, factors significantly associated with overall mortality were an advanced clinical stage, a T4 lymphocytes percentage below 15% and the year of initiation of HAART (before 2005) [15]. The early use of antiretroviral drugs has made the deaths of those children rare in Europe [19]. In addition, Peacock-Villada et al. [22] showed in a comparative study that the average rate of deaths among children under HAART was significantly lower in developed countries than in developing countries. In this comparison, the T4 lymphocytes and viral load were also better in developed countries, this is likely due to delayed HAART initiation in low-income countries. For Wamalwa et al. [23] in Kenya, anemia with hemoglobin less than 9 grams/deciliter was independently predictive of mortality in children receiving the HAART.

In this descriptive study, we determined the overall rates of survival in children under HAART irrespective of associative factors including the WHO clinical stage at the HAART initiation, the T4 lymphocytes level, the nutritional status of children, the co-infections and the socioeconomic status of parents. Globally, the survival rates of children on HAART at 12 months is superimposed on that of adults (94%) [8], and shows the access to HAART programs importance in African countries in terms of years of life saved.

Indeed, Edmonds et al. [24] in Democratic Republic of Congo (DRC) found after adjustment for confounding factors that HAART reduces the risk of mortality by 75% in children treated compared to untreated children. These results in DRC are similar to those found in Europe, in United States and in South Africa [25,26], and confirm that the mortality of HIV-infected children can be reduced in low-income countries if the policy of universal access to HAART is accompanied by the fight against malnutrition, proper management of co morbidities, and specially early initiation of HAART. In this study, screening was done mainly in case of clinical signs, children screened in the PMTCT centers accounted for only 35% of cases. This suggests that efforts should be continued in routine screening of pregnant women in PMTCT centers in Togo. Indeed, in 2010, the rate of coverage of PMTCT services was 33% and only 30% of pregnant women expected in the country have been tested and antiretroviral prophylaxis was offered to 52% of those women [8]. As part of the program for the elimination of the mother-to-child HIV transmission in 2015, the Togolese Ministry of Health has recently developed a national strategy for the rapid expansion of the PMTCT services, as well as the early detection of HIV by PCR. In addition, the application of the new guidelines for HAART in pregnant women and children will firstly reduce the rate of mother-to-child HIV transmission and also significantly improve the care of HIV-infected children.

Conclusion

This study showed that the survival rate of HIV-infected children on HAART was gradually improving since 2007. But, the antiretroviral drugs initiation is delayed because the diagnostic was done after the onset of clinical signs for most children. The country needs to accelerate the expansion of interventions and the provision of PMTCT services in order to decrease the morbidity and mortality of HIV in Togolese children.

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