

SHORT REPORT

Trend of Antiretroviral therapy interruption in a clinic cohort of HIV-infected children in Jos, Nigeria

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Abstract

ABSTRACT

Background: In the early years of introducing antiretroviral therapy (ART), compromised adherence to ART in children, from treatment interruptions, was a challenge partly due to lack of trained or experienced personnel with expertise in adherence counselling. Over subsequent years with increasing expertise coupled with more patient education and public awareness it is expected that these interruptions would decline. We therefore determined the trend in ART interruptions in a clinic cohort of HIV-1 infected children attending the Jos University Teaching Hospital (JUTH).

Methods: This was a retrospective analysis of data on 580 children, aged 2 months – 15 years, who were enrolled on ART between February 2006 and December 2010 at JUTH. Children who had ART interruptions were compared with those who did not. The odds of ART interruption versus no ART interruption, across the categories of year enrolled on ART were examined using the test of homogeneity of odds.

The trend in ART interruptions over a period of 5 years was examined using score test for trend of odds.

Results: The overall frequency of ART interruptions per child among the 580 study subjects over a period of 5 years was 20.2%, that is, 4.04% per year. The odds of ART interruptions was different across the years from 2006 to 2010 ($p = <0.0001$). There was also evidence for a trend in the decreasing odds of ART interruptions over the years ($p = <0.0001$).

Conclusion: ART interruptions declined over the years in children attending the HIV clinic and this may have been due to enhanced ART adherence as a result of repeated health education and decreasing HIV stigmatization.

Keywords: Antiretroviral therapy interruptions, Trend, HIV-1, Adherence, Health education

Introduction

Since the introduction of antiretroviral drugs (ARVs) for the treatment of human immunodeficiency virus (HIV) infection, many countries in sub-saharan Africa (SSA) have continued to scale-up antiretroviral therapy (ART). The benefits of ART in children, which include reduction in morbidity and mortality, are well documented.^{1,5}

In the early years of introducing ART, compromised adherence to ART in children, from treatment interruptions, was obviously a challenge due to several reasons; one of which was the lack of trained or experienced personnel to provide care for children with HIV⁶, amongst others like drug formulation and dosage regimen.⁷ One of the important aspects of HIV care is

adherence counseling, and in general, patient education on the disease.⁶ Over subsequent years with more trained and experienced personnel who would provide more patient education and coupled with more public awareness, it is expected that ART interruption among HIV infected children would be on the decline. This study, we sought to examine the trend in ART interruptions in a cohort of HIV-1 infected children attending the Jos University Teaching Hospital, over a period of 5 years.

Material and Methods

Study design

This was a retrospective analysis of data on 580 children who were consecutively enrolled on ART between February 2006 and December 2010. Study subjects were aged 2 months -15 years diagnosed with HIV-1 infection at presentation to the AIDS Prevention Initiative in Nigeria (APIN)-supported paediatric HIV clinic at the Jos university teaching hospital (JUTH), Jos, Nigeria and who were subsequently commenced on first-line ART. A written informed consent was obtained from the parents/ guardians of the children for use of the data for research and the study was approved by the Ethics committee of the Jos University Teaching Hospital. After HIV diagnosis, prior to commencing ART,

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children and their caregivers were given adherence counseling. During each subsequent monthly follow-up visit, a general health talk was given and again the importance of ART adherence was emphasized to the children and their caregivers.

The diagnosis of HIV and the criteria for commencement of ART in children was based on the Nigeria's National Guidelines for Paediatric HIV and AIDS Treatment and Care.⁸ Children diagnosed with HIV were placed on first-line ART which could be any one of the following combinations: Zidovudine (AZT) + Lamivudine (3TC) or (AZT) + Lamivudine (3TC) + Nevirapine; and the dosing regimen were twice a day.

The adherence counselling was done by trained adherence counsellors and trained Nurses who were themselves trained in the early years of the APIN HIV care programme, by professional adherence counsellors from the Harvard School of Public Health, Boston, MA, USA.

In this study, ART interruption was defined as failure to take medications (missed more than 2 doses or missed more than 1 day of ART within 30 days), whereby ART adherence was < 95%^{6,9}, during any 1 month follow-up period. Each child had a total of 7 follow-up visits over a period of 8 months. And the common reasons for interrupting treatment included: forgetting to take medication, caregiver travelled and medicine not available. The Information on ART interruption was obtained by Caregiver report/patient self-report through direct questioning and captured in the patient standardized Patient Management and Monitoring (PPM) form, specifically this is the Paediatric Follow-up Clinical Encounter form, designed by the Nigeria National Task Team on Paediatric ART and validated by the Harvard School of Public Health.

Statistical analysis

ART interruption was the outcome variable. Children who had ART interruption were compared with those who did not. The analysis on ART interruptions were in two categories:

1. Comparison of ART interruption versus No ART interruption across year of enrollment on ART (2006 – 2010). For this analysis, one ART interruption per child was used (and not multiple interruptions). The odds of ART interruption versus no ART interruption, across the categories of year enrolled on ART were examined using the test of homogeneity of odds. Also, the trend in ART interruptions over a period of 5 years was examined using Score test for trend of odds.

2. Trend in the total number of ART interruptions in a cohort of children each year, over a period of 5 years (2006 – 2010). For this analysis, we used the total number of ART interruptions (multiple interruptions) per child over a period of 7 months follow-up, for each year. The total number of ART interruptions per year was then plotted against the years (2006 to 2010).

All analyses were carried out using Stata software version 10.0 (Stata Corporation, College Station, Texas, USA) and the tests were two-sided with a p-value of <0.05 considered statistically significant. A graph was plotted using Microsoft Office Excel (Microsoft Office 2007), to examine the trend in ART interruptions over the period of 5 years.

Results

The overall frequency of ART interruptions per child among the 580 study subjects over a period of 5 years (2006-2010) was 20.2%, that is 4.04% per year. ART interruptions were more in children aged 1-10 years (75.2%) and more among females (56.4%) as shown in Table 1.

Table 1. Baseline characteristics of HIV infected children interrupting antiretroviral therapy

Characteristics	Antiretroviral therapy interruption			P value*
	Subjects Total N (%)	Yes N (%)	No N (%)	
Age (yrs)				0.51
<1	73 (12.6)	14 (12.0)	59 (12.8)	
1-5	297 (51.4)	54 (46.1)	243 (52.7)	
6-10	147 (25.4)	34 (29.1)	113 (24.5)	
>10	61 (10.6)	15 (12.8)	46 (10.0)	
Median (IQR)	3.5 (1.8-6.6)	3.8 (1.9-7.0)	3.4 (1.7-6.4)	0.28†
Sex				0.08
Male	295 (50.9)	51 (43.6)	244 (52.7)	
Female	285 (49.1)	66 (56.4)	219 (47.3)	
Year enrolled on ART				<0.001
2006	145 (25.0)	50 (42.7)	95 (20.5)	
2007	160 (27.7)	30 (25.6)	130 (28.1)	
2008	122 (21.0)	21 (18.0)	101 (21.8)	
2009	93 (16.0)	13 (11.1)	80 (17.3)	
2010	60 (10.3)	3 (2.6)	57 (12.3)	

*P value for chi squared test †P value for the difference between two median values

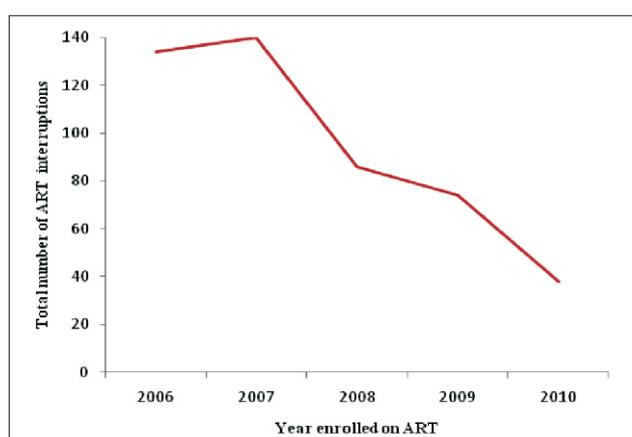
The odds of treatment interruptions was different across the years from 2006 to 2010 ($p = <0.0001$). There was also evidence for a trend in the decreasing odds of ART interruptions over the years from, 2006 to 2010 ($p = <0.0001$) as shown in Table 2.

The frequency of ART interruptions also declined steadily over the period of 5 years (Figure 1).

Table 2. The odds and trends of ART interruptions in HIV infected children over five years

Year enrolled on ART	ART interruption N	No ART interruption N	Odds of ART interruption (95% CI)
2006	50	95	0.53 (0.37 - 0.74)
2007	30	130	0.23 (0.15 - 0.34)
2008	21	101	0.21 (0.13 - 0.33)
2009	13	80	0.16 (0.09 - 0.29)
2010	3	57	0.05 (0.02 - 0.17)

P = <0.0001 (for Test of homogeneity of odds of ART interruption across the years of enrollment on ART) P = <0.0001 (for Score test for trend of odds of ART interruption across the years of enrollment on ART)

**Figure 1. Frequency of ART interruptions over a period of five years**

Discussion

ART interruptions declined over the five year period from 2006 to 2010. This decline in ART interruptions may be due to several reasons. One of these was the repeated health education, including the importance of adherence to ART, which was given to children and their caregivers during monthly clinic visits. Studies have shown that patient education before commencing ART and during follow-up visits, improves adherence to ART.^{10,11}

Another reason may be the increased public awareness on HIV/ AIDS over the years. This has helped in reducing the stigmatization of the disease which in turn could have enhanced regular clinic follow-up visits and adherence to ART.

Over the years of follow-up visits, some of the children grew older and their HIV status was subsequently disclosed to them. It has been shown that subsequent disclosure helps to enhance ART adherence in children.¹² This may have been another reason for the decline in ART interruptions over the years observed in this study.

One of the limitations of our study was that other confounding variables like socio-economic and cultural

factors⁶, as well as the use of fixed dose combination (FDC) antiretroviral drugs⁷ which are known to influence ART adherence, were not studied. The FDC drugs enhance adherence.⁷ Since, FDC drugs were not introduced for use by the study subjects during the study period, until near the end of 2010, it was not a likely confounder of the findings of this study.

Conclusion

Antiretroviral therapy interruptions declined over the years in a cohort of children attending the JUTH paediatric HIV clinic and this may have been due to enhanced ART adherence as a result of repeated health education and decreasing HIV stigmatization. We recommend that ART adherence should be emphasized during follow-up visits in all health care settings providing ART services.

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References

1. Ciaranello AL, Chang Y, Margulis AV, et al. Effectiveness of pediatric antiretroviral therapy in resource-limited settings: a systematic review and meta-analysis. *Clin Infect Dis.* 2009;10:1915–1927.
2. Puthanakit T, Oberdorfer A, Akarathum N, et al. Efficacy of highly active antiretroviral therapy in HIV-infected children participating in Thailand's national access to antiretroviral program. *Clin Infect Dis.* 2005;10:100–107.
3. Patel K, Hernan MA, Williams PL, et al. Long-term effectiveness of highly active antiretroviral therapy on the survival of children and adolescents with HIV infection: a 10-year follow-up study. *Clin Infect Dis.* 2008;10:507–515.
4. Musoke PM, Mudiope P, Barlow-Mosha LN, et al. Growth, immune and viral responses in HIV infected African children receiving highly active antiretroviral therapy: a prospective cohort study. *BMC Pediatr.* 2010;10:56.
5. Ebonyi AO, Oguche S, Dablets E, Sumi B, Yakubu E, Sagay AS. Effect of HAART on growth parameters and absolute CD4 count among HIV-infected children in a rural community of Central Nigeria. *Niger J Paed.* 2014; 41: 1-6.
6. WHO. Adherence to long-term therapies- evidence for action. <http://whqlibdoc.who.int/publications/2003/9241545992.pdf>. (Accessed 22/02/2013).
7. Bangalore S, Kamalakkannan G, Parkar S, Messerli FH. Fixed-Dose Combinations Improve Medication Compliance: A Meta-Analysis. *Am J Med.* 2007;120:713–719.
8. Federal Ministry of Health: Nigeria: National Guidelines for Paediatric HIV and AIDS Treatment and Care. 2010. http://www.aidstarone.com/sites/default/files/treatment/national_treatment_guidelines/Nigeria_peds_2010_tagged.pdf. (Accessed 15/02/2013).
9. Sherr L, Lampe FC, Clucas C, et al. Self-reported non-adherence to ART and virological outcome in a multiclinic UK study. *AIDS Care.* 2010; 22:939-945
10. Tuldra A, Fumaz CR, Ferrer MJ, et al. Prospective

- randomized two-arm controlled study to determine the efficacy of a specific intervention to improve long-term adherence to highly active antiretroviral therapy. *J Acquir Immune Defic Syndr.* 2000;25:221-228.
11. Knobel H, Carmona A, Lopez JL, et al. Adherence to very active antiretroviral treatment: impact of individualized assessment. *EnfermInfeccMicrobiolClin* 1999;17:78-81.
12. Waugh S: Parental views on disclosure of diagnosis to their HIV-positive children. *AIDS Care.*2003;15:169-176.