



Adherence to HAART in children: results from a questionnaire study of children in PENTA 5 trial

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Background

HAART has changed HIV/AIDS from a severe and acute disease to a chronic disease. Adherence to complex regimens of ART drugs is essential to achieve long term suppression of HIV RNA viral load. (1)

This is difficult in children who rely on parents or caregivers to administer drugs, and also in adolescents. Previous, mainly cross-sectional studies have reported that 40-45% of children are not fully adherent to ART (Watson 1999; Reddington 2000) (2-3).

We report on adherence to ART as reported over time by questionnaires filled in by caregivers of children participating in the PENTA 5 trial.

Methods

PENTA 5 was a randomised partially blinded multicentre comparative trial in previously untreated children age 3 months to 16 years.

The trial is divided into Parts A and B:

All children (part A and B) were randomised to one of 3 dual NRTI regimens, zidovudine (ZDV)+ lamivudine (3TC) or ZDV+ abacavir (ABC) or 3TC+ ABC.

Children in part A (asymptomatic) were also randomised to additional nelfinavir (NFV) or matched NFV placebo (pNFV). Children in part B (symptomatic) all received open-label NFV.

At 4, 12, 24 and 48 weeks caregivers completed a questionnaire.

Adherence was assessed by a question asking about number of doses missed in the previous 7 days. Questions were also asked about difficulties taking individual drugs, the most difficult doses to remember and how much taking HAART interfered with every day life.

The effect of different factors on adherence was analysed using univariate logistic regression, followed by a multivariate model based on all factors significant on univariate analysis at p<0.1. The effect of adherence on response to treatment (viral load <400 copies/ml) was assessed using a logistic regression model.

Results

128 children were enrolled in the trial (73 in Part A, 55 in Part B. 126 were followed to at least week 48. At least one questionnaire was returned from 108 (84%) children.

The total number of questionnaires returned was 266 (3 questionnaires were excluded because the question on adherence was not completed) leaving 263 questionnaires.

Differences between children at baseline with and without returned questionnaires were not significant (data not shown).

1. Adherence to ART therapy

In 194 (74%) questionnaires, full adherence was reported for the previous 7 days.

In the remaining 69 (26%):
63 reported missing 1-3 doses
6 reported missing more than 3 doses.

49 (45%) children reported non-adherence on one or more questionnaires.

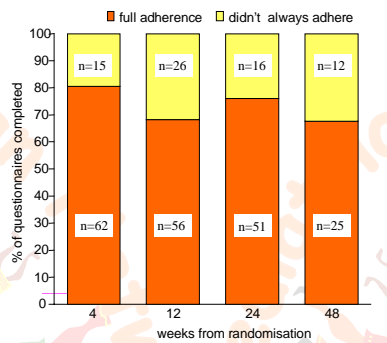
There was a non-significant trend of decreasing adherence over time between weeks 4 and 48 (p=0.2). Ethnicity and the child's knowledge of HIV infection did not affect adherence (n.b. only 8 children knew their HIV infection status)

References

1. Paediatric European Network for Treatment of AIDS. A Randomized Trial to Compare Dual Nucleoside-Analogue Reverse Transcriptase Inhibitor Regimens (ZDV+3TC or ZDV+ABC or 3TC+ABC) With and Without a Protease Inhibitor (Nelfinavir) in Previously Untreated HIV-Infected Children: The PENTA 5 Trial *Lancet* 2002; 359:733-739.
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Figure 1: Reporting of adherence over time



2. Difficulties in taking trial drugs

NFV was reported to be the most difficult drug to take (38% of questionnaires) but the difficulty decreased over time.

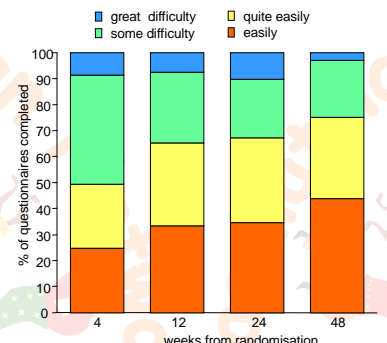
Remembering to take ART was reported to be difficult in 13% of questionnaires and in 31% taking ART was reported to interfere "a lot/quite a lot" with every day life. Taste, smell and size of tablets or liquid were commented on.

The major reason given for forgetting medicines was related to a fear of disclosure (in 22 of 33 caregivers who commented).

IN a univariate and multivariate analysis:

- Children over 10 years were reported to have better adherence compared with children < 5 and 5-10 years old (p=0.04)
- Adherence was worse in children enrolled in part A compared with those in Part B (mainly symptomatic children) (OR 0.53 95% CI 0.29-0.97, p=0.04).

Figure 2: Ease of taking Nelfinavir over time



Collaborators and Acknowledgements

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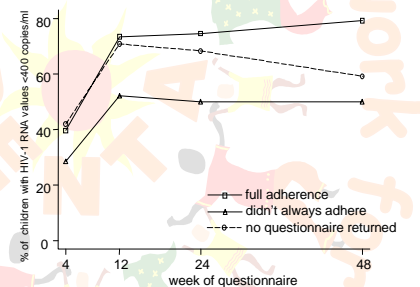
3. Adherence and virological failure

A higher proportion of children reporting full adherence achieved suppression of viral load (< 400 copies/ml), compared with children not completely adherent (p=0.01).

At week 24 and 48 the proportion of children fully adherent with undetectable viral load was 75% and 79% respectively compared with 50% and 50% in children not adherent

There was no evidence of a difference in CD4 response between children who were reported full adherence and those who did not.

Figure 3: Viral suppression and reported adherence



Conclusions

- The level of non adherence found in this study is relatively low compared with other studies conducted in children and remained stable over time.
- Overall 64% of children in the PENTA 5 trial had HIV 1- RNA < 400 copies/ml at week 48 even though around 20% were only on dual therapy (with 2 NRTIs). This underlines the relationship between poor adherence and virological response. No association was found with change in CD4%.
- There was no statistically significant effect on adherence of ethnicity, knowledge of HIV status or whether the carer was also receiving ART.
- Children in part B were more likely to be adherent than those in part A; probably because children who have been ill are more likely to take or be given ART regularly.
- Regarding the relationship between drugs and adherence, Nelfinavir was reported to be the most difficult drug to take, in particular NFV powder, but this decreased over time.
- Many children are unaware of their HIV status and therapy is administered under the control of caregivers.
- Social aspects featured strongly in the comments included on questionnaires. Many comments referred to the problems of trying to preserve confidentiality about the child's HIV diagnosis from others. Caregivers also reported that the need to give HAART regularly impacts negatively on the social life of both the child and their family.

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