

PREVENTION IS BETTER THAN CURE – THE ART OF AVOIDING NON-ADHERENCE TO ANTIRETROVIRAL TREATMENT

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The much-used phrase 'prevention is better than cure' is applicable to many circumstances, including human immunodeficiency virus (HIV) infection. In recent years suggestions have been made for a move towards treatment strategies that emphasise prevention of foreseeable adherence problems on a patient-by-patient basis, through focused patient preparation before commencing antiretroviral therapy (ART). This is well elucidated in a statement made in 2004 by Coetzee *et al.*:¹ 'As it is difficult to ascertain robust predictors of adherence, there has been a move to concentrate on patient preparation before the initiation of ART rather than the use of non-clinical predictors of adherence or selection criteria. A paradigm focused on preparation rather than selection is better suited to the aggressive targets for the scaling up of ART in countries with large epidemics (such as in South Africa), where the view of ART as a very expensive rationed intervention is rapidly changing.'

Strategies for improving patient behaviour and enhancing drug adherence exist but are often complex, requiring much one-to-one patient counselling, and they are often implemented too late, once poor habits have already been established. More value may therefore lie in thorough preparation of patients before commencing ART, rather than adherence interventions once patients are already on treatment. This is not only because consistent and efficacious drug therapy is life saving, but also because drug-resistant strains of HIV emerge in the presence of sub-therapeutic dosing due to sub-optimal adherence.^{2,3} The concept of 'prevention is better than cure' may therefore be applicable to the problem of non-adherence among patients on ART even more than in the management of chronic non-infectious diseases in which drug resistance is not an issue of concern.

We therefore undertook an analysis of results from the adherence monitoring in our HIV care and treatment programme to evaluate whether a change in the focus of conventional HIV treatment strategies would be effective in preventing non-adherence.

BACKGROUND INFORMATION ON THE HIV CARE AND TREATMENT PROGRAMME

Our programme, launched in 2003, is situated in Cato Manor, a ward of the eThekweni (Durban) Metro in KwaZulu-Natal, South Africa, which encompasses

both low-cost housing and informal settlements and is notably an area of low income, with many households and families having no formal income generation.

At the end of November 2008 we had 1 238 patients enrolled in HIV care, with 499 of them on ART (436 adults and 63 children). The programme provides a patient-centred, rights-based, holistic approach to improving and maintaining the wellbeing of HIV-positive mothers, any of their infected family members, and uninfected infants less than 1 year of age. Mothers are generally the primary caregivers in a Cato Manor household, so improvement and maintenance of their health, despite HIV infection, benefits the entire family, as they remain productive and fully functional as caregivers and/or breadwinners. The programme views HIV as a communicable but manageable chronic disease that affects the whole family unit. With a view to keeping family units strong, HIV-positive household members of existing programme participants are eligible for enrolment into HIV care and treatment.

While the approach is to maintain good health before ART is indicated, once eligibility for ART is established patients are prepared, both medically and psychologically, for commencement of treatment according to World Health Organization (WHO) guidelines for the treatment of HIV infection. Medical preparation involves patient examination, evaluation of patient history, exclusion of current tuberculosis

(TB) infection, a full blood count, and kidney and liver function tests. Psychological readiness is assessed by trained HIV counsellors, who conduct drug readiness training before commencement of treatment. Drug readiness training is run over 3 weeks in small-group sessions and includes modules on positive living with HIV infection, preparation for appropriate administration of medicine and adherence to treatment regimens.

METHODS

MONITORING ADHERENCE

Adherence to treatment in adults receiving ART was monitored by pill count at scheduled clinic visits, and expressed as the percentage of the prescribed doses that had actually been taken since the previous visit. Data collected over a 1-year period (December 2007 - November 2008) were analysed monthly, as well as retrospectively at the end of the observation period. At each visit patients were questioned as to whether they were having problems with adherence. Problems with adherence that were identified for specific patients during the course of the year were dealt with at the time by implementing one-to-one adherence counselling, education regarding medication, and the use of any other appropriate aids for helping patients to adhere to treatment.

RESULTS

GENERAL PATIENT DETAILS

At the end of the observation period (end November 2008) there were 499 patients on ART (436 adults and 63 children). Of the adult group, 77 (17.7%) were male and 359 (82.3%) were female, and the mean age was 31.1 years (range 16 - 62 years). Patients had been on treatment in this programme for a mean of 21.2 months (range 1 - 69 months). Twenty-one of the adults on ART were transferred into the programme already on treatment, and had a mean CD4 cell count of 406.3 cells/ μ l on entry to the programme. The 415 treatment-naïve adults who were initiated on ART in our programme had a mean CD4 count of 141.5 cells/ μ l at initiation (range 0 - 675 cells/ μ l).

While paediatric adherence monitoring was done at each visit, only results for the adult cohort were included in this analysis, as the number of children in the programme was comparatively small.

ADHERENCE TO TREATMENT

Analysis of pill count data showed that the mean adherence for every month throughout the year was above 94% and the mean adherence for the patient cohort over the entire observational period was 96.4% (standard deviation (SD) 6.7%), with 90% of patients achieving adherence of 90% or more and 78.5% achieving adherence of 95% or more.

TREATMENT FAILURES AND MORTALITY

During this study (since 2003) 593 patients have been started on ART and there have been 6 treatment failures (1%), necessitating switching of patients to second-line regimens. Thirty-nine patients on ART have died while enrolled in the programme. Two deaths were due to injuries unrelated to ART and were therefore excluded from the deaths for the purposes of this analysis. Thirty-seven deaths were due to opportunistic infections or other HIV-related diseases. None of the patients who died had suffered a known virological treatment failure before death and any changes to the regimen were of single drugs, due to pregnancy, drug toxicity or contraindications. More than half of the deaths occurred within the first 3 months of starting treatment (51%) and 73% within the first year, suggesting that a prominent factor contributing to death was late presentation at the clinic with advanced disease.

EFFECTS OF ADHERENCE INTERVENTIONS AND MONITORING

Mean adherence values for the patient cohort increased throughout the observation period, with the lowest mean adherence (94.2%) reported in the 2nd month of adherence data collection, and the highest (97.4%) in the 11th month. Additionally, the percentage of patients on ART who returned their unused medicine at clinic visits increased each month during the observation period, as patients became more aware of the importance of returning medicine at each visit.

DISCUSSION

It is considered that a 95% adherence rate is required for sustained viral suppression in patients taking protease inhibitor (PI)-based regimens.^{4,5} The mean adherence reported here indicates that medication-taking behaviour for currently used antiretroviral drug regimens was acceptable.

Our programme compares favourably with other studies that report mean adherence measured by medicine returns. A recent South African study in children reported 79% of patients achieving adherence of 90% or more, measured by pill count,⁶ and data from a Botswana study in adults suggested this figure to be 74.4%,⁷ compared with 90% for patients in this programme. A 2003 South African study of HIV-positive adults reported that 63% of patients were 90% adherent or better, while the mean adherence for the patient cohort was 87.2%.⁸ Considering the percentage of patients achieving 95% adherence or more, a large public sector antiretroviral treatment programme in Zambia reported 62.9% of patients with such adherence,⁹ more than 15% lower than the 78.5% of patients in our programme cohort. Two studies on HIV-positive adults in Kenya and Uganda reported similar adherence rates to those achieved in our programme, with 86.1% of patients in standard care achieving 95% adherence or more in the Kenyan

cohort¹⁰ and 87 – 94% (measured at different time points) achieving 95% adherence in the Uganda study.¹¹ Both these studies used medicine returns as well as self-report methods of monitoring adherence.

The favourable adherence values measured over the observation period are evidenced by the low number of treatment failures of first-line ART regimens, and therefore only very few patients being switched to second-line treatment strategies (6 out of 593 patients). Adherence has been shown to have a direct impact on virological suppression^{4,7} and therefore on treatment success, and this is reflected in the positive patient outcomes seen in this programme.

We observed an increase in mean adherence values for the patient cohort throughout the observation period. This improvement in mean adherence correlated with patients' compliance with instructions regarding clinic visits and tablet returns. The mere practice of requesting that unused tablets be returned, and the consistent questioning by pharmacy staff concerning such unused tablets if they are not returned, raised adherence as a point of discussion with patients, resulting in improved patient interaction and better understanding regarding the importance of adherence. The pharmacy staff were given opportunities to discuss specific issues affecting adherence that patients reported when questioned regarding their unused medicine. During the collection of data for adherence measurement, other social and psychological issues surrounding the issue of adherence were identified.

Our data showed that adherence behaviour of patients who returned unused medicine 50% of the time or more (i.e. 6 out of 12 months or more) was better than for those patients who only returned medication at less than 6 visits. Although the difference between the mean adherence for these two groups of patients is not statistically significant, the data may provide a useful tool for highlighting potential adherence problems, as well as a possible area of further research. Pharmacy refill adherence (measured as the percentage of expected pharmacy visits filled) has been shown to predict viral load suppression.¹²

The extended time patients spend in the programme before starting lifelong treatment provides an opportunity for them to observe other patients who are starting treatment, and those who are thriving on ART, which reinforces the trust that is built up over several clinic visits and repeated interactions with programme staff. While still physically well, patients have time to work with counsellors towards accepting their HIV status and adapting their lifestyle to accommodate necessary routines, tasks and habits that will enhance their health, including disclosing their HIV status to family and/or household members. It is during this time

that they become practically and emotionally prepared for starting treatment over the long term. Time to accept their HIV status is important for achieving preparedness for starting ART, and for maintaining good adherence over the long term.

This approach to treatment would be applicable to large-scale implementation in ARV roll-out programmes in resource-poor settings because the staff required to implement the preparative interventions in this programme are at the lay counsellor level. Expansion of the lay counsellor quota of a multidisciplinary team will add less of a financial burden on programme resources than would an increase in clinical staff. Additionally, the employment and training of such lay people provides employment and empowerment to people who live in the community that the programme serves. Employing local residents as lay counsellors enhances knowledge of the community, as well as access into the community and surrounding area, which helps in dealing with difficult patient and family situations through home visits and identification of patients who would otherwise be considered lost to follow-up.

On the basis of our results we conclude that preventing non-adherence is a better treatment approach than strategies in which the primary focus is on identifying and rectifying non-adherence once it has been established. We therefore recommend that HIV care and treatment facilities include such preparative approaches for promoting adherence into their treatment programmes.

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