AIDS briefs

High early mortality after starting antiretroviral treatment in Africa

Patients in sub-Saharan Africa have a high early mortality after starting antiretroviral treatment, according to a review in *AIDS*. Many die within the first 3 months and there was also significant mortality in the interval between being identified as needing treatment and starting therapy.

Around 28% of people who need therapy in the region are now on treatment and initial pessimism over the potential problems of treating patients in the region appear to be unfounded in terms of adherence. However, the high early mortality prompted a review by an international team of investigators who looked at mortality rates, timing, risk factors and causes of death among adults accessing antiretroviral treatment programmes in sub-Saharan Africa.

The team reviewed 18 published cohort studies, which covered more than 35 000 patients treated in 9 countries – mainly through public-access antiretroviral schemes. The median baseline CD4 cell count in these studies ranged from 43 to 147 cells/mm^3, and the duration of follow-up varied between 3 and 46 months. The vast majority of patients had never received antiretrovirals before, and most started treatment with two nucleoside analogues and one non-nucleoside reverse-transcriptase inhibitor.

The team identified that early high mortality was a key challenge in antiretroviral treatment programmes. At 12 months between 8% and 26% of patients who were not lost to follow-up had died. In most cohorts, the mortality rates were high in the first year despite good virological suppression, but then fell in the second year. However, in some cohorts this mortality persisted into the second year. Although this issue has been noted in previous studies the figures in this review are worse than those from earlier studies.

Cohorts in South Africa and Ivory Coast with good verification of outcomes found that, whereas most deaths occurred in the first months of treatment in patients with the lowest baseline CD4 cell counts, losses to follow-up were evenly distributed over time and were not associated with CD4 cell counts. However, if a programme reports high loss to follow-up over initial months of treatment, this could point to high rates of unascertained deaths.

High mortality rates were also found during the period before starting treatment. In Cape Town, one study found that 67% of deaths during the first 3 months occurred in the period between enrolment and starting antiretroviral treatment (approximately 30 days). Another South African cohort reported 87% of deaths prior to starting therapy. These delays are caused by delays in patient referral, waiting lists for antiretroviral treatment and length of patient preparedness programmes. Finding the balance between the time needed to prepare patients for lifelong therapy and starting them on life-saving treatment needs urgent research, according to the authors.

The key risk factors for early mortality were identified as low baseline CD4 counts and advanced disease (WHO Stage 4). Compared with people with higher CD4 cell counts, individuals with a CD4 count of less than 50 cells/mm^3 were two and a half times more likely to die (summary hazard ratio 2.5; 95% CI, 1.9 - 3.2). Compared with WHO stages 1 - 3, WHO stage 4 was also associated with more than a doubling in the hazard of death (summary hazard ratio 2.2; 95% CI, 1.5 - 3.2).

High early mortality (as much as 4-fold) has also been reported from private antiretroviral programmes, possibly due to poor adherence in comparison to public programmes.

Strategies to reduce early mortality include promotion of early HIV diagnosis, strengthening of patient care before and during treatment, laboratory monitoring, timely initiation of treatment and free treatment, and prophylaxis for opportunistic infections. TB is a particular issue and guidelines already suggest early initiation of TB treatment in people with CD4 cells below 100/mm^3.

Lawn SD. *AIDS* 2008; 22:1897-1908.

TB vaccine reduces new cases in HIV-positive people by almost 40%

A tuberculosis (TB) vaccine reduced the incidence of new cases by 37% in a large placebo-controlled randomised clinical trial in Tanzania, according to reports at the World Lung Health Conference in Paris recently.

The reduction was statistically significant, and if it were possible to vaccinate 50% of people diagnosed with HIV in Tanzania, the number of new TB cases in the country could fall by around 3 300 per year, said lead investigator Ford von Reyn.

However, availability of the vaccine in the field is likely to be a long-term prospect. The results came from the DarDar study, which was a phase III study designed to test the safety and efficacy of a TB vaccine in a large population of HIV-positive people, with the intention that if successful, the study results could be used in licensing the vaccine for widespread use.

The vaccine used a whole inactivated mycobacterium, *M. vaccae*, which had already been tested for safety in Europe, North America and Africa. The study started in 2001, recruiting 2 000 people with HIV, 70% of whom were women, with a CD4 count in the range 200 - 500 cells/mm^3. This range was chosen so that participants could mount a response to mycobacteria. The response declines significantly once CD4 counts fall below this range.

Von Reyn CF, *et al.* 39th World Conference on Lung Health of the International Union Against Tuberculosis and Lung Disease, Paris, abstract PS-81689-20, 2008. (Published in *Int J Tuberc Lung Dis* 2008; 12 (11): suppl. 2).