AIDS briefs

An alternative emergency contraceptive

Anna Glasier and colleagues, writing in *The Lancet*, report on a new emergency contraceptive that can be used up to 5 days after unprotected intercourse.

They compared ulipristal with levonorgestrel in women with regular menstrual cycles who presented to a participating family planning clinic requesting emergency contraception within 5 days of unprotected sexual intercourse. A total of 2 221 women were randomly assigned to receive a single, supervised dose of 30 mg ulipristal acetate (*N*=1 104) or 1.5 mg levonorgestrel (*N* =1 117) orally. Allocation was by block randomisation stratified by centre and time from unprotected sexual intercourse to treatment, with allocation concealment by identical opaque boxes labelled with a unique treatment number. Participants were masked to treatment assignment whereas investigators were not. Follow-up was done 5 - 7 days after expected onset of next menses. The primary endpoint was pregnancy rate in women who received emergency contraception within 72 h of unprotected sexual intercourse, with a non-inferiority margin of 1% point difference between groups (limit of 1.6 for odds ratio). Analysis was done on the efficacy-evaluable population, which excluded women lost to follow-up, those aged over 35 years, those with unknown follow-up pregnancy status, and those who had re-enrolled in the study. Additionally, they undertook a meta-analysis of their trial and an earlier study to assess the efficacy of ulipristal acetate compared with levonorgestrel.

The found that in the efficacy-evaluable population, 1 696 women received emergency contraception within 72 h of sexual intercourse (ulipristal acetate, *N*=844; levonorgestrel, *N*=852). There were 15 pregnancies in the ulipristal acetate group (1.8%, 95% CI 1.0 - 3.0) and 22 in the levonorgestrel group (2.6%, 1.7 - 3.9; odds ratio (OR) 0.68, 95% CI 0.35 - 1.31). In 203 women who received emergency contraception between 72 h and 120 h after sexual intercourse, there were 3 pregnancies, all of which were in the levonorgestrel group. The most frequent adverse event was headache (ulipristal acetate, 213 events (19.3%) in 1 104 women; levonorgestrel, 211 events (18.9%) in 1 117 women). Two serious adverse events were judged possibly related to use of emergency contraception; a case of dizziness in the ulipristal acetate group and a molar pregnancy in the levonorgestrel group. In the meta-analysis (0 - 72 h), there were 22 (1.4%) pregnancies in 1 617 women in the ulipristal acetate group and 35 (2.2%) in 1 625 women in the levonorgestrel group (OR 0.58, 0.33 - 0.99; p=0.046).

They conclude that ulipristal acetate provides women and health care providers with an effective alternative for emergency contraception that can be used up to 5 days after unprotected sexual intercourse.

Glasier AF, *et al. Lancet*, early online publication, 29 January 2010, doi:10.1016/S0140-6736(10) 60101-8

Second-line antiretroviral treatment in South Africa shows good results

CAROLE LEACH-LEMENS

High rates of increased CD4 cell counts and viral suppression together with low mortality were seen in adults at a large HIV public sector urban clinic in Johannesburg, South Africa after 1 year on second-line antiretroviral therapy, Fox and colleagues report in a study published online ahead of print in the *Journal of Acquired Immune Deficiency Syndromes*.

In 2007 an estimated 300 000 people were receiving antiretroviral therapy in South Africa as a result of the Government's 2004 large-scale plan for the provision of antiretrovirals. Outcomes for those on first-line regimens have been good. However, there is a growing concern that the number of people failing on treatment will increase as the numbers starting treatment and time on treatment increase.

Furthermore, use of single-dose nevirapine given to women for the prevention of mother-to-child transmission leads to the increased probability of developing resistance, and consequent failure of first-line regimens containing nevirapine.

The anticipated increase in demand for second-line regimens in resource-poor settings raises the question of their long-term effectiveness, and in particular the need to understand who fails second-line treatment and why. The high costs of second-line regimens and concerns about the development of resistance in resource-poor settings where viral load testing is uncommon underscore the importance of this research, yet scant evidence of the effectiveness of second-line regimens in resource-poor settings exists.

A rise in the need for second-line therapy is anticipated in South Africa in the near future. Treatment guidelines for the public sector support switching to a second-line regimen after two consecutive viral loads over 5 000 copies/ml.

A cohort study was undertaken using data from a 4-year period (April 2004 - June 2008) from all patients 18 years of age or older who had begun a standard public sector second-line regimen of zidovudine, didanosine and lopinavir/ritonavir after a standard first-line triple therapy at the Themba Lethu Clinic (TLC) in Johannesburg. The clinic's protocol for switching is based on toxicity or two consecutive viral loads over 1 000 copies/ml.

TLC, one of the largest public HIV clinics in South Africa with nearly 11 000 patients having begun antiretroviral treatment, is located at an urban referral hospital. Since 2006 all care at TLC is given free of charge.

Treatment monitoring includes CD4 counts and viral loads at 4 months after start of a new treatment regimen and then every 6 months thereafter unless clinical assessments indicate otherwise.

The cohort included 328 patients. Data analysis included survival, and immunological and virological outcomes after 1 year of follow-up. The authors chose three measures of treatment success:

- alive and in care (AIC), which they defined as not known to have died nor lost to follow-up (missed a scheduled treatment pick-up for longer than 3 months)
- achieving an undetectable viral load – less than 400 copies/ml, and
- increases in CD4 cell count.

At 1 year of follow-up 78% (243/313) (95% CI 73 - 82) were AIC. However, reaching and maintaining an undetectable viral load is a more precise measure of long-term treatment effectiveness; 77% (203/262) (95% CI 72 - 82) had an undetectable viral load at 1 year.

Time-matched comparisons with those on first-line treatment showed those on second-line were only marginally less likely to be AIC after 1 year (HR 0.84, 95% CI 0.73 -0.97).

The authors note that while their findings are similar to a Médecins sans Frontières (MSF) cohort covering resource-poor countries, a comparison is not really valid. The MSF cohort showed a higher percentage of those AIC at 1 year (86%), but the data included several different second-line regimens, with most participants having been on a first-line regimen of stavudine, lamivudine and nevirapine. Standard first-line treatment in South Africa consists of stavudine, lamivudine and efavirenz.

Even with these considerations the authors stress the positive outcomes for those switched to second-line at 1 year of follow-up.

Mean CD4 cell count increase at 1 year was 133 cells/mm^3. The authors note that this compares favourably with the MSF study and represents a significant immune recovery.

Identification of who fails and why is critical to the ongoing success of second-line regimens. The authors found that patients who were switched before they had a second detectable viral load over 1 000 copies/ml (HR 1.68; 95% CI 1.08 - 2.61) were more likely to reach undetectable viral load at the end of 1 year, as were those who switched for reasons other than non-compliance with first-line treatment (HR 1.83; 95% CI 1.14 -2.93).

The authors highlight that in most resource-poor settings antiretroviral treatment failure is detected by clinical assessment alone. Considerable drug resistance will have already developed. In contrast, this cohort underwent regular viral load monitoring, and so switching probably occurred earlier than with clinical assessment alone. The authors suggest that, as a result, the degree of resistance acquired is limited.

Fox MP, *et al.* High rates of survival, immune reconstitution and virologic suppression on second-line antiretroviral therapy in South Africa. *J Acquir Immune Defic Syndr* (advance online publication) 2010.

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BRIDGET FARHAM

Letter

DDT may cause androgyny in babies

To the Editor: The report 'DDT may cause androgyny in babies – experts' (News Bites, *CME* 2009; 27: 522) is misleading and potentially damaging to malaria control programmes in South Africa and beyond. Chris Bateman reports verbatim comments made by Anthony Turton, alleging that DDT used in malaria control is a cause of androgyny and that 'a high correlation exists between the application of DDT as a (malaria) control measure and the birth of babies with deformed genitalia ... ' . Neither Turton nor Bateman provides scientific references for these claims and so the reader is unable to critically examine the evidence. I am not aware of any scientifically replicated peer-reviewed study that proves that DDT used in malaria control is a cause of androgyny or birth defects – Over many decades DDT has been used in malaria control around the world. Thousands of scientific studies have confirmed that the human health benefits of such use far outweigh any potential human health harm. Furthermore, over several decades thousands of tonnes of DDT were used in agriculture and disease control programmes in wealthy Western countries, such as the USA, Canada and much of Western Europe. Yet there is no evidence from these countries that DDT use resulted in any cases of androgyny or birth defects – outcomes which would have been reported and investigated given the sophisticated health systems that are a feature of these countries. None of the studies purporting to find human health harm caused by DDT satisfies even the most basic epidemiological criteria required to prove cause and effect. Where DDT has been used in malaria control, death rates have fallen sharply and populations have grown. Failure to report on these facts and verbatim reporting of what amounts to wild and unsubstantiated claims is poor journalism at best and dangerous scaremongering at worst.

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