Methods for Improving Reproductive Health in Africa

A phase III trial of the diaphragm and lubricant gel for HIV prevention in women

MIRA

Background

The Methods for Improving Reproductive Health in Africa (MIRA) trial was a multi-site, open-label, randomized controlled trial to determine the effectiveness of the diaphragm and Replens© lubricant gel in preventing heterosexual acquisition of HIV and other STI infections in Zimbabwean and South African women. Both products evaluated in this study are commercially available; the diaphragm has been used by women for decades.

Trial Summary

Enrollment of participants began in August 2003 and the study was completed in December 2006; 5,045 HIV-negative, sexually active women were recruited from clinics and community-based organizations at three sites in South Africa and Zimbabwe. Women attended study clinics for quarterly follow-up visits for up to 24 months (median was 21 months of follow-up). All participants received a comprehensive HIV prevention package consisting of pre-test and post-test counseling about HIV and sexually transmitted infections, testing, treatment of curable sexually transmitted infections, intensive risk-reduction counseling, and provision of condoms. During the trial, free hormonal contraceptives were made available to participants. Half of the participants were randomly selected to receive, in addition, an Ortho All-Flex© latex diaphragm and a non-contraceptive lubricant (Replens© gel). The primary outcome of the MIRA trial was incident HIV infection.

Key Findings

Finding 1: HIV Outcome

Overall HIV annual incidence in the trial was 4.0%. There was no statistical difference in the rate of new HIV infections in the two study groups: in the intervention group (those who received a diaphragm plus lubricant along with male condoms) 158 out of 2,472 women became HIV infected (a 4.1% HIV incidence per 100 woman-years) whereas in the control group (those who received male condoms only) 151 out of 2,476 women became HIV infected (a 3.9% HIV incidence per 100 woman-years). Therefore, the study findings do not support the addition of the diaphragm to current HIV prevention strategies.

While there was high condom uptake among all study participants, uptake was lower in the intervention group than in the control group. On average, the proportion of last sex acts where women reported using male condoms was 54% in the intervention group compared to 85% in the control group ($p<0.0001$). However, the lower reported condom use among women provided with diaphragms did not result in increased infection, a finding which merits further research.

Reporting of adverse events was similar between the two groups, confirming that the study products are safe. Rates of pregnancy were the same in both groups, with an overall annual incidence of first pregnancy of 13.1%.

Finding 2: Other STI Infections Outcome

There were 471 first *Chlamydia trachomatis* (CT) infections and 192 first *Neisseria gonorrhoeae* (GC) infections among the 4,968 participants who had at least one follow-up urine sample for CT/GC analysis; overall incidence of CT and GC in the trial was 6.2 and 2.4 per 100 woman-years, respectively. Intention-to-treat analysis found no statistical difference in the rate of new CT or GC infections in the two groups. However, in a separate analysis that examined the effect of the intervention among those who reported "always use" of the diaphragm since the last quarterly visit as compared to those who reported use less than always, there was a statistically significant reduction in the incidence of GC among women in the intervention group as compared to those in the control group (RH 0.61, 95% CI: 0.41-0.91). These findings do not support the addition of the diaphragm to current STI prevention strategies, though they do suggest that consistent use of the diaphragm may reduce GC acquisition.

MIRA Study Products

There were 210 herpes simplex virus type 2 (HSV-2) infections among 2,016 trial participants who were HSV-2 seronegative at enrollment; overall incidence of HSV-2 in the trial was 6.8 per 100 woman-years. There was no statistical difference in the rate of new HSV-2 infections in the two groups. These findings do not support the addition of the diaphragm to current STI prevention strategies.

Other Findings

In addition to the main study publications related to HIV and other STI infection outcomes, additional analyses of the MIRA trial data have addressed diaphragm and condom acceptability, covert use of HIV prevention technologies, vaginal practices, contraception use and effectiveness, prevention trial recruitment and retention, and discrepancies in diagnosis of incident HIV infection between antibody-based and DNA-based tests, among others. A full list of publications from the trial through May 2011 follows.

Cervical Barrier Advancement Society

Main Study Publications

Padian NS, van der Straten A, Ramjee G, Chipato T, de Bruyn G, Blanchard K, Shiboski S, Montgomery ET, Fancher H, Cheng H, Rosenblum M, van der Laan M, Jewell N, McIntyre J, the MIRA Team. Diaphragm and lubricant gel for prevention of HIV acquisition in Southern African women: a randomized controlled trial. *Lancet*. July 2007; 370(9583):251-261.

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Other Study Publications

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The MIRA trial was supported by a grant from the Bill and Melinda Gates Foundation. Dr. Nancy Padian of the Women's Global Health Imperative (formerly at UCSF, now at RTI International) was the trial's principal investigator, and the collaborating institutions and co-investigators were:

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This brief will be updated on an ongoing basis as analysis of the MIRA data continues and publications become available. For more details about the MIRA trial visit the Cervical Barrier Advancement Society (CBAS) at www.cervicalbarriers.org. At CBAS you'll also find more background information, fact sheets, and explanatory documents about clinical trials and cervical barrier methods.

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