Methods for Improving Reproductive Health in Africa
A phase III trial of the diaphragm and lubricant gel for HIV prevention in women

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.

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). This finding does 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.

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.
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Main Study Publications


Venkatesh K, van der Straten A, Mayer KH, Blanchard K, Ramjee G, Lurie MN, Chipato T, Padian NS, de Bruyn G. African women recently infected with HIV-1 and HSV-2 have increased risk of acquiring N gonorrhoeae and C trachomatis in the MIRA trial. *Sexually Transmitted Diseases*.