Study identifies superior drug regimen for preventing mother-to-child HIV transmission

18 November 2014

For HIV-infected women in good immune health, taking a three-drug regimen during pregnancy prevents mother-to-child HIV transmission more effectively than taking one drug during pregnancy, another during labor and two more after giving birth, an international clinical trial has found.

The ongoing PROMISE (Promoting Maternal-Infant Survival Everywhere) study also has found that one triple-drug regimen for preventing mother-to-child transmission may be safer than another for women and their babies.

These findings provide further support for World Health Organization guidelines for preventing mother-to-child HIV transmission, according to the researchers. The findings were reported on Nov. 4, 2014 during a scheduled interim review of the PROMISE study data by an independent data and safety monitoring board (DSMB).

"We now have the gold standard of evidence—data from a randomized clinical trial— supporting a three-drug regimen as the preferred approach for preventing HIV transmission from an infected mother to her baby during pregnancy and delivery," said Anthony S. Fauci, M.D., director of the National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health. "This is another important step in our efforts to define the best approaches toward the goal of eliminating of mother-to-child HIV transmission globally."

"The new findings strongly support the recommendation by WHO and most countries to provide a three-drug anti-HIV regimen to all pregnant women with HIV infection," added George Siberry, M.D., a medical officer in the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) at NIH.

The PROMISE study, which began in 2010, aims to determine how best to safely reduce the risk of HIV transmission from infected pregnant women to their babies during pregnancy and after delivery. It also aims to learn how stopping versus continuing a triple-drug anti-HIV regimen after breastfeeding affects mothers who are in good immune health. The study has enrolled more than 3,500 HIV-infected pregnant or post-partum women who did not meet national criteria for receiving anti-HIV treatment and more than 3,200 HIV-exposed infants of these women in India, Malawi, South Africa, Tanzania, Uganda, Zambia and Zimbabwe.

The International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) network is conducting the study with funding from NIAID and NICHD. The National Institute of Mental Health at NIH also funds the IMPAACT network. Protocol chair Mary Glenn Fowler, M.D., M.P.H., of the Makerere University-Johns Hopkins University Research Collaboration in Kampala, Uganda, and Johns Hopkins University School of Medicine in Baltimore, leads the study.

The component of the study that yielded the new findings was examining which of two proven strategies is safer and more effective at preventing mother-to-child HIV transmission before and during delivery:

giving women zidovudine as early as 14 weeks into the pregnancy, a single dose of nevirapine during labor, and two weeks of tenofovir and emtricitabine after delivery (called Option A by WHO); or giving women one of two triple anti-HIV-drug regimens as early as 14 weeks into the pregnancy (part of what WHO calls Option B and Option B+).

At the time of the DSMB review, more than 3,500 women in good immune health had been assigned at random to receive either Option A or one of these three-drug regimens: lamivudine, zidovudine and ritonavir-boosted lopinavir (the lamivudine combination) or tenofovir, emtricitabine and ritonavir-boosted lopinavir (the tenofovir

combination).

The DSMB concluded that there was a significantly lower rate of mother-to-child HIV transmission during pregnancy or delivery among the women who received a three-drug regimen during pregnancy than among those who received Option A. Only 0.5 percent of infants whose mothers received the lamivudine combination and 0.6 percent of infants whose mothers received the tenofovir combination became infected with HIV, while 1.8 percent of infants whose mothers received Option A became infected.

The DSMB also concluded that the lamivudine combination was safer than the other regimens. Women who received the lamivudine combination had fewer severe adverse pregnancy outcomes (such as very low birth weight, very premature delivery, stillbirth, spontaneous abortion or major birth defects) than women who received the tenofovir combination. In addition, fewer babies whose mothers received the lamivudine combination died within two weeks of birth than did those whose mothers received the tenofovir combination or Option A. The most common reported cause of these deaths was prematurity.

However, there were more adverse pregnancy outcomes of lesser severity—specifically, birth weights of less than 2,500 grams (5 pounds 8 ounces) and preterm delivery at fewer than 37 weeks gestation—among babies whose mothers received a triple-drug regimen than among babies whose mothers received Option A.

In light of the findings, NIAID has accepted the DSMB's recommendation that the results be made public and that the team consult with women in the study who remain pregnant and with their health care providers to determine the best HIV preventive regimen. The rest of the study will continue as originally designed. The participating women and children are being followed until two years after the last child is born to address questions about the safety and efficacy of anti-HIV drug regimens taken during the breastfeeding period. The study also is assessing maternal health after the breastfeeding period among women in good immune health who either stop or continue taking triple-drug anti-HIV regimens.

All infants are receiving a daily dose of nevirapine until 6 weeks of age, and those who acquire HIV infection from their mothers are being given combination anti-HIV therapy.

"The PROMISE study team looks forward to completion of the trial to determine the most effective and safest strategies for preventing mother-to-child HIV transmission during breastfeeding and for optimizing the health of HIV-infected mothers and their babies," said Dr. Fowler.

Provided by NIH/National Institute of Allergy and Infectious Diseases