New treatment regimen cuts severity of drug-resistant malaria in pregnancy

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Credit: CDC

A two-drug preventive treatment greatly reduces the severity of malaria during pregnancy, according to a study funded by the National Institutes of Health. The treatment provides an alternative for many parts of Africa where the malaria-causing parasite *Plasmodium falciparum* has grown resistant to standard treatment.

Pregnancy lowers the body's defenses against malaria-causing parasites. Malaria during pregnancy increases the risk for maternal and infant death. However, even in areas where mothers have a high level of immunity, malaria parasites can infect the placenta, robbing the fetus of nutrients and increasing the chances for low birth weight, preterm birth and infection.

The two-drug regimen, dihydroartemisinin-piperaquine, appeared to provide a reliable alternative to the standard treatment, sulfadoxine-pyrimethamine, for the study participants. The authors note that in sub-Saharan Africa, malaria during pregnancy is responsible for up to 20 percent of low birth weight deliveries and more than 100,000 infant deaths each year.

The study appears in the *New England Journal of Medicine*. It was conducted by Abel Kakuru, M.D., of the Infectious Diseases Research Collaboration in Uganda, Grant Dorsey, M.D., Ph.D, of the University of California, San Francisco, and colleagues at Makerere University College of Health Sciences, in Kampala, Uganda.

"On average, pregnant women living in the study area endure an estimated 310 bites from malaria-carrying mosquitos each year," said Rohan Hazra, M.D., chief of the Maternal and Pediatric Infectious Disease Branch at NIH's Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), which funded the study. "This drug combination appears to offer a welcome addition to our defenses against this debilitating and life-threatening disease."

The study enrolled 300 pregnant women from Tororo, Uganda from June through October, 2014. All were age 16 or older, ranging from 12 to 20 weeks pregnant. The women were assigned at random to one of three groups for preventive treatment. The first received dihydroartemisinin-piperaquine at three intervals: 20, 28 and 30 weeks

of pregnancy. The second group received the same drug combination, but once each month. The comparison group was given sulfadoxine-pyrimethamine, the standard treatment, at 20, 28 and 30 weeks of pregnancy. Participants had monthly checkups at the study clinic, where they received regular blood tests for malaria.

The researchers evaluated the women for malarial infection in the placenta, a diagnosis made by finding parasites in the placenta at the time of birth or by observing the presence of pigment the parasite deposits in tissue after it digests blood cells. The researchers confirmed placental malaria in 50 percent of the women in the sulfadoxine-pyrimethamine group. Among the group receiving three doses of dihydroartemisinin-piperaquine, 34.1 percent had placental malaria, compared to 27.1 percent in the monthly treatment group.

Many of the women who did not have symptoms of malaria during pregnancy nonetheless had malaria pigment in the placenta. However, heavy deposits of the malaria pigment were more likely to occur in the sulfadoxine-pyrimethamine group and least likely to occur in the monthly dihydroartemisinin-piperaquine group.

The researchers also evaluated the women and infants in the study for a composite adverse birth outcome of spontaneous abortion, stillbirth, low birthweight, preterm delivery or birth defects. Risk of any adverse birth outcome was lower in the monthly dihydroartemisinin-piperaquine group (9.2 percent) than in the three-dose group (21.3 percent) or the sulfadoxine-pyrimethamine group (18.6 percent).

The researchers concluded that monthly dosing of dihydroartemisinin-piperaquine provided the best protection against malaria and called for additional studies to determine if the drug combination would provide an effective alternative treatment in other parts of Uganda and elsewhere in Africa.

More information: Kakuru, Abel et al. Dihydroartemisinin-Piperaquine for the Prevention of Malaria in Pregnancy. *New England Journal of Medicine*, 2016.