Widely used malaria treatment to prevent malaria in pregnant women

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A global team of researchers, led by a research team at the Liverpool School of Tropical Medicine (LSTM), are calling for a review of drug-based strategies used to prevent malaria infections in pregnant women, in

areas where there is widespread resistance to existing antimalarial medicines.

Professor Feiko ter Kuile, an expert in malaria in pregnancy, recently worked with a multi-disciplinary team including the US Centers for Disease Control and Prevention, the WorldWide Antimalarial Resistance Network (WWARN) and Duke University to complete the most comprehensive study to date of the impact of sulphadoxine-pyrimethamine (SP) drug resistance on the effectiveness of intermittent preventative treatment (IPTp).

Published today in *Lancet Infectious Diseases*, the results demonstrate that the clinical effectiveness of SP in protection of pregnant women against malaria is compromised in certain areas. The experts call for further urgent investigation into alternative strategies or drugs to prepare for further growing resistance to this mainstay of preventive therapy.

The WHO recommends intermittent preventive treatment (IPTp) in malaria endemic areas. The only antimalarial currently recommended for IPTp is SP; to date IPTp with SP has effectively resulted in reductions in maternal anaemia, low birth weight and neonatal mortality. However, with the growing threat of drug resistance emerging or spreading in sub-Saharan Africa, this protection is now at risk.

It is estimated that without protection during pregnancy, 45% of 32 million pregnancies in malaria endemic sub-Saharan Africa are exposed to Plasmodium falciparum malaria, leading to 900,000 malaria-associated low birthweight deliveries. Low birth weight, anaemia and other serious adverse birth outcomes result in numerous longer-term health issues for infants.

Prof ter Kuile from LSTM comments, "We reviewed more than 100,000 birth outcomes across Sub-Saharan Africa, our results suggest that the

widely used antimalarial SP for preventive therapy remains very effective in many parts of Africa, but that there is a clear trend toward reduced effectiveness with increasing levels of resistance by the malaria parasite to SP. In areas with the highest grade of resistance where more than 37% of parasites carry six mutations in the so-called pfdhfr and pfdhps genes, the effectiveness of SP appears to be fully compromised. It is clear that in these high resistance settings alternative approaches to the prevention of malaria in pregnancy are urgently needed to achieve better birth outcomes for pregnant women."

Carol Sibley, WWARN's Senior Scientific Advisor from the University of Washington, adds, "This large-scale analysis has given us a powerful message: the increasing prevalence of molecular markers of SP is correlated with a decrease in effectiveness of SP to reduce low birth weight and malaria infections.

We also have a clear recommendation that molecular monitoring of parasites in humans is a valuable tool for policy makers to monitor the spread of antimalarial resistance and assess the impact on this valuable prevention strategy for malaria in pregnancy and therewith on the lives of newborns in low income settings across Africa."

Since resistance evolves by a series of mutations in the parasite, molecular monitoring of parasites in humans can support policy makers and health professionals to make important decisions about the need for alternative prevention options.

Anna Maria van Eijk, first author concludes, "We are also calling for further analysis into the potential additional benefits that SP may continue to have even in areas where it is no longer able to kill malaria parasites. For example, through its anti-microbial effects, or perhaps SP has some anti-inflammatory and immune modulating effects that are similar to those discovered for widely used antibiotic cotrimoxazole.

This is important as SP may not work as well as other antimalarials in high SP resistance areas, but it may still be able to help reduce poor birth outcomes, such as low birth weight through these other mechanisms.

We hope that by examining the risks, outcomes and alternative strategies available we will ensure that vulnerable babies born in low resource settings are given the best possible chance of good health, by receiving the most effective antimalarial prevention approaches and medicines available to us today, and in the future."

Provided by Liverpool School of Tropical Medicine