

Mefloquine fails to replace SP for malaria prevention during pregnancy

September 23 2014

In today's issue of *PLOS Medicine*, Clara Menendez from the Barcelona Institute for Global Health (ISGlobal), Spain, and colleagues report results from two large randomized controlled trials conducted in Africa to test an alternative drug for malaria prevention in HIV-negative and HIV-positive pregnant women.

Pregnant women and their unborn children are at a high risk for complications from [malaria](#) infection, and finding new treatment options is important because the malaria parasites are becoming increasingly resistant to the existing WHO-recommended drug sulphadoxine-pyrimethamine (SP). In addition, SP-based treatments are not recommended for HIV-positive women because of problematic interactions between SP and a drug called cotrimoxazole which is routinely given to HIV-positive individuals to prevent secondary infections.

Suitable drugs for intermittent preventive treatment during pregnancy (IPTp) must be safe for the mother and the fetus and able to be given during regular antenatal care visits while providing long-lasting protection. The antimalarial drug mefloquine (MQ) is a candidate thought to meet these criteria, and is not known to interact with cotrimoxazole.

The first trial (González, Mombo-Ngoma, et al.) compared the currently recommended IPTp regimen with two different formulations of MQ in 4,749 HIV-negative [pregnant women](#). The second trial (González, Desai,

et al.) compared three doses of MQ with a placebo in 1,017 HIV-positive pregnant women who also received cotrimoxazole. The main outcome of trial 1 was the frequency of children born with low [birth weight](#). The main outcome in trial 2 was the frequency of women with malaria parasites in their blood (parasitemia) at delivery. Both trials also measured adverse pregnancy outcomes (such as miscarriage or stillbirth), other indicators of maternal health during pregnancy, and drug tolerability.

Both trials found that MQ can reduce malaria infections and improve overall health in pregnant women, compared to either SP (trial 1) or placebo (trial 2). However, results from trial 1 indicate that neither of the two MQ regimens was better than SP at preventing low birth weight, and tolerability for MQ was poorer than for SP (with more participants in the MQ groups reporting nausea and dizziness). Trial 2 showed that MQ recipients had less parasitemia than placebo recipients, no difference in adverse pregnancy outcomes or in [low birth weight](#) between the two groups, and poorer tolerability in the MQ group than the placebo group. Trial 2 also found that women in the MQ group had higher HIV viral loads at delivery than women in the placebo group and were more likely to transmit HIV to their child around the time of birth. As this result was based on an unplanned exploratory analysis, the question of whether MQ interferes with HIV suppression needs to be studied further before definite conclusions can be drawn.

In view of their results, the authors conclude that MQ at the dose used in this study cannot be recommended as an alternative to SP in HIV-negative pregnant women, nor for [malaria prevention](#) during pregnancy in HIV-positive women. In an accompanying Perspective, Richard Steketee (PATH, Seattle, USA) agrees: while the [trials](#) confirmed that MQ is safe during pregnancy and showed that the drug can reduce rates of [malaria infection](#) and maternal illness, the lack of obvious benefit for fetal health and the poor tolerability are barriers to recommending MQ..

Nonetheless, pointing to related studies under way and arguing that attention on how to protect pregnant women and their fetuses from malaria must continue, Steketee concludes that "by likely closing a door on IPTp with mefloquine, [the research presented in the two papers] opens other doors for further important work in the coming years".

More information: Gonza'lez R, Mombo-Ngoma G, Oue'draogo S, Kakolwa MA, Abdulla S, et al. (2014) Intermittent Preventive Treatment of Malaria in Pregnancy with Mefloquine in HIV-Negative Women: A Multicentre Randomized Controlled Trial. *PLoS Med* 11(9): e1001733. [DOI: 10.1371/journal.pmed.1001733](https://doi.org/10.1371/journal.pmed.1001733)

Steketee RW (2014) Malaria Prevention during Pregnancy—Is There a Next Step Forward? *PLoS Med* 11(9): e1001734. [DOI: 10.1371/journal.pmed.1001734](https://doi.org/10.1371/journal.pmed.1001734)

Gonza'lez R, Desai M, Macete E, Ouma P, Kakolwa MA, et al. (2014) Intermittent Preventive Treatment of Malaria in Pregnancy with Mefloquine in HIVInfected Women Receiving Cotrimoxazole Prophylaxis: A Multicenter Randomized Placebo-Controlled Trial. *PLoS Med* 11(9): e1001735. [DOI: 10.1371/journal.pmed.1001735](https://doi.org/10.1371/journal.pmed.1001735)

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