Most effective malaria drug regimens highlighted in study

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Image courtesy of Rowan McOnegal, Wellcome Images

A study published today identifies the most effective drug combinations recommended for use as first-line treatments for malaria. The research also suggests that augmenting the treatments with a single dose of the drug primaquine could have a major effect on malaria transmission from treated patients and play a crucial role in elimination programmes.

Malaria kills more than a million people each year, mainly young children and pregnant women. It is caused by parasites that are injected into the bloodstream by infected mosquitoes. The most deadly form, Plasmodium falciparum, is responsible for nine out of ten deaths from malaria.

The most effective antimalarial drug is artemisinin, derived from Artemisia annua, also known as sweet wormwood, which had been used in Chinese medicine for centuries under the name Qinghaosu. It was rediscovered in the 1970s, evaluated first in South-east Asia, and

eventually accepted as an essential component of antimalarial treatment in the past few years.

Although antimalarial drugs - most commonly in the form of the derivative artesunate - can be used on their own as a monotherapy, fears over the possible development of resistance mean that they are usually given in conjunction with one or more other drugs as artemisinin-based combination therapies (ACTs) - now recommended by the WHO as the first-line treatment for uncomplicated falciparum malaria in all endemic countries.

Researchers based at the Wellcome Trust-Mahidol University-Oxford Tropical Medicine Research Programme carried out an open-label randomised trial in clinics in Myanmar (Burma) to compare the effectiveness of all four WHO-recommended fixed-dose ACTs - artesunate-amodiaquine, artemether-lumefantrine, artesunate-mefloquine and dihydroartemisinin-piperaquine - as well a loose tablet combination of artesunate and mefloquine.

Their findings, published online today in 'The Lancet Infectious Diseases', show that three of the four fixed-dose treatments and the loose-tablet combination were highly effective. The only exception was artesunate-amodiaquine, which they say should no longer be used as a first line treatment in Myanmar.

The researchers also trialled the addition of a single dose of the drug primaquine, which targets gametocytes in the blood. The gametocyte is the developmental stage of the parasite that can be transmitted by and to the mosquito. They found that primaquine substantially cut the length of time that gametocytes remained in the blood, thus reducing the potential of the malaria parasite to be retransmitted.

"We hope that our study will provide evidence on which policy-makers

can base their decisions regarding which drug regimens should be used for first-line treatments," says Professor Nick White, a Wellcome Trust Principal Research Fellow who is based in Bangkok, who led the study.

"We recommend that artesunate-amodiaquine is no longer offered for treatment in Myanmar, but also recommend the addition of a single dose of primaquine. This latter drug is highly effective at clearing the blood of the malaria parasite and could have a major effect on malaria transmission from treated patients. It could play a crucial role in elimination programmes."

More information: Smithuis, F et al. Effectiveness of five artemisinin combination regimens with or without primaquine in uncomplicated falciparum malaria: an open-label randomised trial. *Lancet Infectious Diseases*; e-pub 9 Sept 2010.

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