Less effective antimalarial therapies can help fight malaria better

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Credit: CDC

Oxford University scientists have found that the more effective way to beat malaria is to use less effective drugs some of the time.

The current drug of choice for malaria - artemisinin - is extremely effective at saving lives from the disease, but artemisinin-resistant malaria parasites are spreading as the drug is used more and more. A

computer simulation study now suggests that treating malaria in a population by simultaneously using a non-artemisinin therapy amongst more effective artemisinin-based combinations is the best way to combat the disease, while still reducing the spread of drug-resistant malaria. Writing in the *Lancet Global Health*, scientists at the Nuffield Department of Clinical Medicine at Oxford University found that this combination worked best even when the non-artemisinin drug was only effective 85% of the time in treating malaria.

Currently, to stop the spread of artemisinin-resistant parasites, the World Health Organization (WHO) encourages the use of the drug in combination with other anti-malarials; the malaria parasite would have to become simultaneously resistant to both the drugs in order to survive this two-hit artemisinin combination therapy.

However, malaria parasites in South-East Asia have begun to acquire characteristics to help evade even this double hit, and these resistant strains are likely to spread over the next decade as the use of artemisinin combination therapies becomes more widespread.

Health policy makers are therefore in bind, having to decide whether to safeguard artemisinin effectiveness (by avoiding its overuse), or to encourage the use of artemisinin wherever possible to save people's lives.

Professor Maciej Boni and his colleagues ran computer simulations to find out if there was an optimal strategy that could stop the spread of drug-resistant malaria parasites across populations, while still effectively treating malaria in individual patients. They found that simultaneously dosing a population with several artemisinin-combination therapies - say, by prescribing artemisinin in combination with different partner drugs on different days of the week - was more effective than either cycling between different artemisinin combination therapies, or by sticking to one specific combination until the combination started failing.

The simulation also found that if this simultaneous dosing also included a combination without artemisinin, malaria parasites that were resistant to artemisinin were slower to emerge, and slower to spread. Including this potentially less effective treatment option didn't necessarily mean that many more people would not recover from malaria: in the worst case scenario of the non-artemisinin treatment being only 75% as effective as artemisinin combination therapy, fewer than 7% of malaria patients would still have post-treatment malaria parasites in their blood as a result of not being prescribed an artemisinin drug.

Professor Boni said, 'For this subgroup of patients, second-line treatment with an artemisinin combination therapy would be recommended. The ethical implications of such a treatment policy will need to weighed against the benefit of delaying and slowing down the spread of artemisinin resistance.

'But the nightmare we all want to avoid is the establishment of artemisinin resistance in Africa, where hundreds of millions of individuals rely on artemisinin-based therapies as their first-line antimalarial treatment. By deploying different antimalarial therapies simultaneously - including non-artemisinin-based therapies - national malaria control programs in Africa should be able to slow down the spread of artemisinin-resistant parasites when they are imported into the continent.'

More information: Tran Dang Nguyen et al. Optimum population-level use of artemisinin combination therapies: a modelling study, *The Lancet Global Health* (2015). DOI: 10.1016/S2214-109X(15)00162-X

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