

Malaria treatment could improve in children

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An analysis of patients from across the malaria endemic world suggests that a key antimalarial treatment could be improved by better dosing in young children.

Antimalarial <u>drug resistance</u> has hampered <u>malaria control</u> programs for almost 60 years. A key factor in combatting this threat is to ensure that all <u>antimalarial drugs</u> are deployed in a way that ensures that the maximum number of patients are completely cured.

A study published this week in *PLOS Medicine* explores this issue by presenting the results of a large pooled analysis of more than 7,000 patients with malaria from Africa, Asia and South America. It presents a convincing argument for public health policy-makers to pay careful attention to dosing recommendations for artemisinin combination therapies (ACTs) when reviewing current drug <u>treatment</u> protocols, particularly for <u>young children</u>.

The paper examines the combination of piperaquine and dihydroartemisinin, an increasingly common choice of treatment for patients suffering from malaria caused by the malaria parasite *Plasmodium falciparum*.

The results of the study, coordinated by the WorldWide Antimalarial Resistance Network (WWARN), show that while treatment of malaria with dihydroartemisinin-piperaquine generally results in excellent patient recovery, young children are at higher risk of treatment failure and this may be due to their receiving an insufficient dose of the drug.



WWARN brought together 76 researchers worldwide who contributed individual patient data from 26 clinical studies. These data are being used to analyze the implications of different drug dosing levels of ACTs, for treatment efficacy. The results, which combine almost 70% of all available published data on this treatment, confirm that dihydroartemisinin-piperaquine is highly efficacious curing more than 97% of patients.

However, the study also highlights that one third of children aged 1-5 years received a dose of piperaquine below that recommended by the World Health Organisation. Furthermore, patients receiving a lower dose were slower to respond to treatment and had a greater risk of getting malaria again.

Dr Corine Karema, from the Rwandan National Malaria Control Program and a co-author of the paper, emphasises that "It is very important that treatment guidelines recommend optimal drug dosing levels to maximise their impact and ensure all patients are rapidly and completely cured."

The results suggest that further drug dose optimization of dihydroartemisinin-piperaquine may be warranted in young children.

Professor Ric Price, one of the lead investigators working with WWARN, concludes "This study highlights the ability of researchers from around the world to come together and pool their data for collective gain. The power of such research collaborations will help to support the optimisation of current antimalarial treatments, reduce the spread of antimalarial drug resistance and ultimately save lives"

In a linked Perspective, Paul Garner, from the Liverpool School of Tropical Medicine, UK, discusses some of the issues associated with optimizing ACT dosing.



He says: "There is a balancing act between under-dosing, which increases the risk of resistance developing, and increasing dosing such that toxicity and adverse events increase."

More information: The WorldWide Antimalarial Resistance Network (WWARN) DP Study Group (2013) The Effect of Dosing Regimens on the Antimalarial Efficacy of Dihydroartemisinin-Piperaquine: A Pooled Analysis of Individual Patient Data. *PLoS Med* 10(12): e1001564. <u>DOI:</u> 10.1371/journal.pmed.1001564

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