Antimalarials less effective in malnourished children

The most-prescribed antimalarial drug is less effective in severely malnourished children, a University of Cape Town (UCT) study shows. The study calls for further research into optimising treatment for undernourished children - who are particularly vulnerable to contracting and dying from the disease.

Image: World Vision International

“Although one in three children under five years old in sub-Saharan Africa is malnourished, they are usually excluded from studies on malaria treatment,” says Professor Karen Barnes from the UCT Division of Clinical Pharmacology. She, along with Associate Professor Lubbe Wiesner and Michiel Smit, collaborated with international partners on the research.

The physiology of malnourished children may change the way antimalarial drugs are taken up and distributed by their bodies. Malnutrition could, for instance, reduce the absorption of drugs in children, but there has been little research into how well the treatments work for them. The information available seems to be contradictory.

“The dosage regimens recommended for these children don’t seem to be optimal and this increases the chances that treatment will fail for them – which is what we showed in this study,” says Barnes, who is also head of the Worldwide Antimalarial Resistance Network Pharmacology Group and the founding director of the South African Medical Research Council’s Collaborating Centre for Optimising Antimalarial Therapy.

Artemether-lumefantrine is the most commonly used antimalarial drug worldwide. Scientists have already recorded, though,

that levels of the drug – which is recommended by the World Health Organisation – are lower in children's blood, compared to adults', after treatment. Despite this, children are currently given the same dose as adults, adjusted for their body weight.

The team analysed how the drug behaved over time in terms of absorption, distribution, metabolism and excretion (its pharmacokinetics) as well as its effectiveness (its pharmacodynamics). To do this, they looked at data for 399 children (all with malaria, 131 of them severely malnourished) involved in a clinical trial at two hospitals in Mali and Niger. The concentrations of the drug were measured by Wiesner's team using an assay developed and validated by Smit.

Developing optimal drug dosages

"This study is the first to address the challenge of treating malaria in severely malnourished children, specifically," says Barnes. "It highlights how important it is to make sure that optimised drug doses are developed for undernourished children and other vulnerable groups – such as pregnant women – who are usually excluded from studies to decide treatment doses." These groups are often excluded from clinical trials, as they may not represent the main target group, they are difficult to recruit and their participation can raise ethical concerns.

The results showed that not only were the levels of lumefantrine lower in children's blood compared to adults', but that among severely malnourished children there was even less of the drug – about 19% less – than in other children. This lower exposure also meant these children acquired new malaria infections sooner.

The researchers explored increasing, intensifying and extending this treatment. The model showed that increasing the dosage would not result in increased exposure, because of the limited ability of severely malnourished children to absorb the drug. However, both the intensified regimen (three times a day for three days) and an extended regimen (twice a day for five days) brought the exposure up to levels similar to those in the other children.

"Now we need to test these in malnourished young children," Barnes concludes. "This is so that treatment guidelines can align with the optimal malaria treatment for the very many young and malnourished children living in malaria areas in sub-Saharan Africa."

Source: University of Cape Town