Combination drug treatment can cut malaria by 30 percent

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Malaria infections among infants can be cut by up to 30 per cent when antimalarial drugs are given intermittently over a 12 month period, a three-year clinical trial in Papua New Guinea has shown.

The trial showed the drug regime was effective against both *Plasmodium falciparum* and Plasmodium vivax malaria, the first time antimalarial drugs have been shown to prevent infections by both species of malaria. The treatment regime, called intermittent preventive treatment (IPT), protected the infants against malaria for at least six weeks after the end of treatment, showing that it had an ongoing protective effect and did not hinder the development of natural immunity.

The study was led by Professor Ivo Mueller from the Walter and Eliza Hall Institute and Barcelona Centre for International Health Research (CRESIB) with Dr Patricia Rarau and Dr Nicolas Senn from the Papua New Guinea Institute of Medical Research (PNGIMR). Professor Peter Siba from PNGIMR, Associate Professor Louis Schofield from the Walter and Eliza Hall Institute, Professor John Reeder and Dr James Beeson from the Burnet Institute and Professor Stephen Rogerson from the University of Melbourne also collaborated on the project.

Professor Mueller, from the Walter and Eliza Hall Institute's Infection and Immunity division, said the findings could lead to trials of IPT in other regions, including South-East Asia and South America, where malaria, particularly *P. vivax*, is a major health problem. IPT has been used for number of years in sub-Saharan Africa, where more than 80 per

cent of all deaths from malaria are in children under the age of five.

"*Plasmodium vivax* is the main cause of clinical malaria in infants outside of Africa," Professor Mueller said. "What this study has shown is that IPT can be useful in regions other than sub-Saharan Africa, that it can be an effective tool against *P. vivax*, and reaffirms that we need to effectively tailor preventive drugs to different malaria species in different regions."

IPT uses sporadic, short courses of combined antimalarial drugs to provide protection against malaria infection. "IPT is a cheap and easy way to decrease the burden of malaria in those most susceptible to clinical illness, such as young infants and pregnant women," Professor Mueller said.

As part of the clinical trial, infants aged three to 15 months were treated with a long-lasting antimalarial drug combination at three, six, nine and 12 months. Professor Mueller said the most effective drug combination in the trial was the long-lasting antimalarials sulfadoxine/pyrimethamine and amodiaquine (SP-AQ), which act against the two most lethal species of malaria parasite, *Plasmodium falciparum* and *Plasmodium vivax*. In the trial, SP-AQ treatment decreased infant infections by 35 per cent for Plasmodium falciparum and 23 per cent for *Plasmodium vivax*.

"These are quite remarkable figures," Professor Mueller said. "Different treatment strategies are required for different regions, depending on the dynamics of disease. The drug combination that was most effective in PNG was very different to the drugs you would use to treat malaria in Africa and also different to the drugs currently recommended for treating malaria in PNG."

Professor Peter Siba, director of PNGIMR, said a key factor in the effectiveness of the treatment was running it in parallel with existing

vaccination and healthcare programs.

"In the trials, IPT was given at the same time as regular vaccinations and check-ups, using existing health care frameworks to deliver the treatment, so we saw a much higher adherence than with continuous treatment regimes. IPT is also preferable to long-term, continued use of antimalarial drugs, as it allows some natural immunity to develop while decreasing the number and severity of malaria infections," Professor Siba said.

Provided by Walter and Eliza Hall Institute