Year-round preventive treatment reduces malaria risk in young children

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Credit: CDC

A year-round preventive drug treatment substantially reduces young children's risk of contracting malaria and poses no serious risk of adverse events, according to a study by researchers funded by the National Institutes of Health.

The findings demonstrate that prolonged treatment given from 6 to 24

months of age is safe and effective for young children, according to the study authors. Year-round preventive measures are badly needed in locations like Uganda, where the study took place, and where malaria rates remain high throughout the year.

Most previous studies using drug treatment to prevent malaria have been limited to areas where there is only a seasonal risk of the disease, during the rainy season, when most malaria episodes in children occur. In those studies, preventive drug treatment was given for only a few months at most. The current study demonstrated that continuous preventive treatment can substantially reduce malaria transmission to infants, who are at greatest risk of severe malaria and death.

The study was conducted by Grant Dorsey, M.D., of the University of California, San Francisco (UCSF) at San Francisco General Hospital, with colleagues from UCSF and the Infectious Diseases Research Collaboration, Kampala, Uganda, and Makerere University College of Health Sciences, also in Kampala. The researchers published their findings online in *PLOS Medicine*.

"This study has identified an effective measure for reducing the incidence of malaria in children living in an area with high rates of the disease," said Lynne Mofenson, M.D., chief of the Maternal and Pediatric Infectious Disease Branch at the NIH's Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), which provided funding for the study.

Dr. Mofenson said malaria poses a greater threat to children below 3 years of age than to older children. Malaria in children under age 3 is more likely to be fatal than in older children. In younger children, also, the disease may affect the brain and either prove fatal or result in brain damage.

"It's better to try to prevent a potentially fatal illness than it is to wait until the child gets the illness and is at increased risk for dying," Dr. Mofenson added. Older children are considered to be less at risk from malaria because they tend to develop natural immunity against the disease as they get older.

The researchers found that a monthly dose of dihydroartemisinin-piperaquine (DP) was the most effective of three anti-malaria drugs at reducing malaria risk in children from 6 months to 24 months of age. The other two study drugs— monthly sulfadoxine-pyrethamine (SP) or daily trimethoprim-sulfamethoxozole (TS)— have been in use longer, and in many locations the malaria-causing parasite has developed a resistance to them. The researchers conducted the study to determine if the benefits of treatment outweighed the potential risk of anemia and other side effects from the drugs.

"When you're giving drugs to prevent the disease, you have a much higher bar for safety," Dr. Dorsey said. "When the drugs are given longer term, you may have an increased risk of side effects to contend with."

Beginning at age 6 months, 393 children from Tororo, Uganda were randomized to one of four groups: monthly DP, monthly SP, or daily TS, or to a control group, which did not receive any preventive drug treatment—which is the standard medical practice in the area. Insecticide-treated mosquito bed nets are a mainstay for reducing the spread of malaria, and all of the families were given nets to put over the children when they slept. By 24 months of age, 352 children were still taking part in the study.

The researchers calculated the study results in terms of a numerical unit known as person years, which takes into account the number of individuals participating in the study and the time each person took part.

(A study following 1,000 people for 1 year would contain 1,000 person years of data.) For the children in the DP group, there were 3.02 malaria episodes per person year, 5.21 for the TS group, 6.73 for the SP group, and 6.95 for the control group. Compared to the control group, children in the DP group were 58 percent less likely to develop malaria. Between the groups, there was no difference in rates of anemia and other adverse events that have been associated with the drugs used in the study.

After discontinuing the study drugs at age 24 months, the researchers followed the children until age 3 and found no difference in malaria rates between the groups. According to the study authors, the findings help to allay any concerns resulting from earlier studies that continuous drug treatment might interfere with the children's ability to develop an immune response against malaria, and so make them more likely to get the disease after treatment stops.

"Our study showed that preventive drug treatment can greatly reduce malaria in young children in areas where there are year round high rates of transmission," Dr. Dorsey said. "We believe that this treatment regimen will be of substantial benefit in many parts of the world in need of improved malaria control measures."

More information: Bigira V, Kapisi J, Clark TD, Kinara S, Mwangwa F, et al. (2014) Protective Efficacy and Safety of Three Antimalarial Regimens for the Prevention of Malaria in Young Ugandan Children: A Randomized Controlled Trial. *PLoS Med* 11(8): e1001689. doi:10.1371/journal.pmed.1001689. www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1001689

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