Sickle cell anemia treatment does not increase malaria risk in Africa

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The drug hydroxyurea does not appear to increase the risk of malaria infection in patients with sickle cell anemia who live in malaria-endemic regions, according to a study published online today in *Blood*, a Journal of the American Society of Hematology (ASH).

Sickle cell anemia (SCA) is an inherited disorder characterized by abnormal red blood cells that stick together in patients' blood vessels, blocking the blood flow to organs, which can lead to severe pain, organ failure, stroke, and even death. In low-resource regions of sub-Saharan Africa, more than 50 percent of children with SCA die before the age of five.

Hydroxyurea, a medicine recommended for children with SCA in high-resource settings like the United States and Europe, is not widely prescribed in sub-Saharan Africa, which has the highest burden of SCA in the world. This is partly because of a lack of data that hydroxyurea will be effective and safe in low-resource regions. In particular, some research suggests that hydroxyurea could make people with SCA more susceptible to malaria , a serious and sometimes fatal disease spread by mosquitoes and common across sub-Saharan Africa.

"Research has been unclear over whether the changes in immune response caused by hydroxyurea could increase the risk of malaria," said Chandy John, MD, of Indiana University School of Medicine, principal investigator of the trial. "Because hydroxyurea provides such positive outcomes for people in high-resource regions, we want to be sure that this drug is safe for children in low-resource, malaria-prone settings.

To understand if hydroxyurea use is associated with higher rates of malaria in sub-Saharan Africa, researchers from the United States and Uganda established the Novel use Of Hydroxyurea in an African Region with Malaria (NOHARM) trial, a year-long, randomized double-blinded placebo-controlled study.

NOHARM was led on the ground by co-principal investigator Robert O. Opoka, MMED, of Makerere University in Kampala, Uganda. The team recruited 208 children aged 1-4 years and randomly assigned them into one of two treatment arms, in which they received either a fixed dose of hydroxyurea or a placebo for a full year. All patients also received standard bed netting and anti-malaria medication.

"Not only were we pleased to see that the overall incidence of malaria was low, but there was also no correlation between hydroxyurea treatment and the rate or severity of malaria," said co-principal investigator and head of data coordination Russell E. Ware, MD, PhD, of Cincinnati Children's Hospital Medical Center.

The treatment arms did not differ in terms of incidence or severity of malaria infection or other adverse events. Three children on hydroxyurea experienced a total of five malaria episodes, while seven of those receiving placebo had a total of seven malaria episodes. Two children in the hydroxyurea arm died, one from presumed sepsis and the other from unknown sudden death; one child in the placebo arm died, presumably from sepsis.

Children receiving hydroxyurea also had lower rates of pain crises and hospitalizations. "Because the children prescribed hydroxyurea experienced significantly better outcomes without any increase in malaria risk, we are incredibly encouraged to further explore the drug's use in sub-Saharan Africa," said Dr. Ware.

As overall malaria incidence was low in the NOHARM study population, it will be important to monitor the rate and severity of malaria with hydroxyurea use in areas of higher malaria

transmission. Drs. John, Ware, and Opoka are currently in the process of recruiting participants for a follow-up study to gauge the optimal dose for children with SCD in resource-limited, malaria-prone regions.

"It is our hope that these research studies can help establish hydroxyurea as the standard of care for children with sickle cell disease in Africa," said Dr. John.

Provided by American Society of Hematology