MedicalXpress

Statin drug shows promise for fighting malaria effects

December 27 2012

Researchers have discovered that adding lovastatin, a widely used cholesterol-lowering drug, to traditional antimalarial treatment decreases neuroinflammation and protects against cognitive impairment in a mouse model of cerebral malaria. Although there are differences between mouse models of cerebral malaria and human disease, these new findings indicate that statins are worthy of consideration in clinical trials of cerebral malaria, according to an article published in the Dec. 27 issue of *PLOS Pathogens*.

Malaria, a parasitic infection that is transmitted to humans by the female Anopheles mosquito, is one of the leading infectious diseases worldwide. Cerebral malaria is a severe, potentially fatal neurologic complication of infection by the parasite Plasmodium falciparum. Studies of children with cerebral malaria show that cognitive deficits, such as impaired memory, learning, language, and mathematical abilities, persist in many survivors long after the infection itself is cured.

"Over 500,000 children develop cerebral malaria each year in sub-Saharan Africa, and persistent cognitive dysfunction in survivors is not only a major public health concern, but also a significant socioeconomic burden," says Guy Zimmerman M.D., associate chair for research in the Department of Medicine at the University of Utah and senior co-author on the study. "There is an urgent and unmet medical need for therapies that treat or prevent cognitive impairment in cerebral malaria."

Statins, a class of drugs best known for their ability to lower cholesterol,

have also been shown to be active in modulating a variety of immune system responses. In their research, Zimmerman and his Brazilian colleagues evaluated the effect of statins in a mouse model of cerebral malaria. The researchers found that adding a drug called lovastatin to traditional antimalarial therapy prevented cognitive dysfunction in mice infected with cerebral malaria. They discovered that addition of lovastatin decreased white blood cell accumulation and leakiness in blood vessels in the brain. Lovastatin also reduced production of damaging oxygen-containing molecules and other factors that promote inflammation.

"The molecular mechanisms that give rise to cerebral malaria and subsequent cognitive dysfunction are not yet known," says Zimmerman. "However, the fact that statin treatment decreases both injurious blood vessel inflammation and cognitive dysfunction suggests that a combination of vascular and inflammatory triggers leads to cerebral pathology and intellectual deficits."

Zimmerman and his colleagues also studied lovastatin in an experimental model of bacterial sepsis, a severe whole-body inflammatory state that can also lead to cognitive impairment. They found that lovastatin also prevented cognitive impairment after bacterial sepsis.

"Our findings are exciting because the clinical implications extend beyond cerebral malaria to other severe systemic inflammatory syndromes complicated by brain involvement," says Zimmerman. "We believe our observations are the first experimental evidence to support the possibility of using statins to reduce cognitive impairment in critically ill patients."

Provided by University of Utah Health Sciences