Nitric oxide impacts source of sickle cell pain crisis

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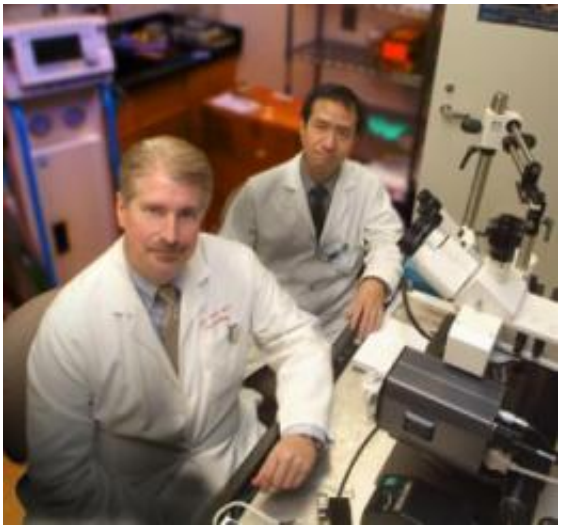

Nitric oxide gas appears to directly impact the source of the classic, disabling pain crises of sickle cell disease, Georgia Health Sciences University researchers report. Dr. C. Alvin Head, Chairman of GHSU's Department of Anesthesiology, and Dr. Tohru Ikuta, GHSU molecular hematologist, collaborated on the research. Credit: Phil Jones, GHSU, Campus Photographer

Nitric oxide gas appears to directly impact the source of the classic, disabling pain crises of sickle cell disease, Georgia Health Sciences University researchers report.

The short-acting gas helps unglue hemoglobin molecules that stick together, forming long chains that ultimately deform red blood cells and

prompting a cellular pileup in small blood vessels and pain, said Dr. C. Alvin Head, Chairman of GHSU's Department of Anesthesiology.

The findings get scientists closer to understanding why red blood cells sickle and potentially to a easy-to-use, non-addictive treatment that helps avoid it, said Dr. Tohru Ikuta, GHSU molecular hematologist.

Hydroxyurea, which prompts the body to make more fetal hemoglobin which cannot sickle, is currently the only approved therapy for sickle cell. Patients with recurring pain crises typically must take increasingly higher doses of stronger narcotics to deal with the pain.

Head and his colleagues envision instead an inhaler like asthmatics use that enables them to breathe in nitric oxide when they feel a pain crisis coming on. "Drugs just mask the symptoms," Head said. "We have mounting evidence that nitric oxide directly addresses the source of pain crises to help patients avoid them."

They've shown in a small patient sample that inhaling nitric oxide appears safe and effective. The study of 18 patients in Atlanta, Chicago and Detroit published in 2010 in the American Journal of Hematology showed that the half who inhaled nitric oxide for four hours had better pain control than those receiving only the standard self-administered morphine.

The new study examined nitric oxide's impact from many angles and showed that it appears to disperse dense, solid chains of hemoglobin troublemakers. Once a significant number of hemoglobin molecules stick together, it causes red blood cells to distort from their natural round shape that easily maneuvers blood vessels to a sickle-shape. At that point, red blood cells also become uncharacteristically sticky.

They found nitric oxide reduced the length of the unnatural hemoglobin

strands, made the strands more fragile and, using a high-powered confocal microscope, they could see it also helped cells regain a more normal shape. Studies were done on human cells in vitro.

Next steps include fine-tuning the dose and learning more about why red blood cells become sticky. Head notes that with a gas, it's a lot more tricky to determine how much drug gets into the blood than with an oral or intravenous delivery. They already have evidence that in sickle cell disease red and white blood cells stick together, which they should not.

They believe their findings about how these cells clog up vessels will have broad applications for a number of clot-based conditions, including the increased clot risk that follows surgery. "Really what we are learning is the basic understanding of early clot formation," Head said.

Provided by Georgia Health Sciences University

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