Study probes genetic link to sickle cell pain management

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Dr. Cheedy Jaja, nurse research scientist and Assistant Professor of Biobehavioral Nursing in the GHSU College of Nursing, is studying genetic links to pain in sickle cell disease. Credit: Phil Jones, GHSU Photographer

A study that may help personalize pain medication management for sickle cell disease patients is underway at Georgia Health Sciences University.

Dr. Cheedy Jaja, a nurse research scientist and Assistant Professor of Biobehavioral Nursing, has received a three-year National Institutes of Health grant to determine if variations in genes known to play a role in metabolizing opioids could help physicians manage sickle cell pain.

The World Health Organization estimates that 275,000 babies are born with sickle cell disease each year. It is most common among African-Americans and people of Hispanic, Mediterranean, Caribbean or Southeast Asian descent.

In the United States, approximately 100,000 people have the disease, including one in four blacks. About 30 percent of patients don't respond well to analgesics prescribed for the debilitating episodic pain that is a hallmark of sickle cell disease.

"They have to go to the emergency department for help," Jaja said. "This core group keeps coming back and coming back."

Health care providers risk misidentifying these patients as drug seekers.

"Sickle cell is a lifelong condition in which a pain crisis can be triggered at any time," Jaja said. "The sad part is that two individuals may have the same disease, but how they experience pain differs vastly. So understanding this difference is critical in understanding how to manage the disease. These are simple questions in sickle cell research that have not been explored."

Ineffective pain management can predispose patients to increased drug tolerance or dependence.

Jaja, who completed a postdoctoral fellowship in pharmocogenetics at Indiana University before obtaining master's degrees in public health genetics and nursing from the University of Washington, had a "what if" moment during his emergency department rotation.

"It could be that the medication they've been given is not adequate," he thought. "Maybe this pain is a manifestation of their genetic makeup."

Jaja knew that genetic polymorphisms in three cytochrome P450 enzymes vary from patient to patient, resulting in different metabolism rates – poor, efficient, intermediate and ultra-rapid.

Jaja considered it "just common sense" to determine what gene variation patients have and use that information to determine which drug at what dosage would provide optimal relief.

"The idea is to identify patients who are most likely to experience severe pain and target them for aggressive personalized care with a preventive medication approach," Jaja said.

He will follow 100 adult patients at GHSU's Sickle Cell Center in Augusta and satellite clinics in Albany, Macon, Savannah and Valdosta. In addition to defining gene variations that determine how pain medications are metabolized, he will track emergency department visits and medication prescriptions, theorizing that poor and rapid metabolizers will be hospitals' "frequent fliers." Jaja also has a GHSU Child Health Discovery Institute pilot grant to examine the same issue in 30 pediatric patients.

If correct, said Jaja, "We will be on the cutting edge of treatment for our patients. This will change the current prescription practice to one of targeted intervention."

Jaja, originally from Sierra Leone, a country in West Africa where sickle cell disease is rampant and treatment facilities are rudimentary to non-existent, saw many of his childhood friends die from the disease, fueling his desire to study its treatment and management.

Jaja came to GHSU in 2008 to work with mentor Dr. Abdullah Kutlar, Professor of Hematology/Oncology and Director of the GHSU Sickle Cell Center, a comprehensive internationally recognized center for sickle

cell treatment and research. The center incorporates the work of faculty from medicine, pediatrics, hematology/oncology, neurology, molecular biology and other specialties in a multidisciplinary approach to patient care, research and education. It serves as the core laboratory for several multicenter trials.

GHSU has earned international acclaim through the years for its advances in sickle cell treatment, including identification of various hemoglobin abnormalities; the impetus for nationwide newborn screening of hemoglobin abnormalities; the use of blood transfusions to minimize stroke risk in children; and more recently, the treatment potential of nitric oxide and a thalidomide analog.

"This is a sickle cell research paradise," Jaja said.

Kutlar is conducting a similar study looking at variants of the mu-opioid receptor gene present in the brain that metabolize analgesics, while Jaja's research focuses on enzymes in the liver and stomach that metabolize opioids.

"Our vision ultimately is to use genetic information on drug-metabolizing enzymes as a standard of care to improve quality of life in medically vulnerable patients," Jaja said. "The converging synergy between our studies will further analgesic selection for sickle cell disease pain management."

Jaja's grant, a Mentored Research Scientist Development Award, includes an intense training component that will prepare him to become an independent translational research scientist.

He will work closely with Dr. Martha Tingen, Professor at the Georgia Prevention Institute, Dr. Ferdane Kutlar, Director of the Sickle Cell Center Laboratory; Dr. Roger Vega, Section Chief of Pediatric

Hematology/Oncology; and Dr. Matthew Lyon, Associate Professor of Emergency Medicine.

As a new investigator, Jaja was selected for the Functional Genomics of Blood Disorders Program of the National Heart, Lung, and Blood Institute's 2009 Summer Institute Program to Increase Diversity in Health-Related Research.

He is a member of the Pharmacogenetics Research Network, the Pharmacogenetics Knowledge Base, the American Pain Society Sickle Cell Pain Group, the International Association of Sickle Cell Nurses and Physician Assistants and the International Society of Nurses in Genetics.

Provided by Georgia Health Sciences University