Methadone provides pain relief for kids with sickle cell

October 10 2016, by Judy Martin

Former study patient Anntenisha Toler speaks with Jennifer Horst, MD, about her battles with pain caused by sickle cell disease. Horst co-authored a study that found that a single dose of methadone, added to standard pain-killing drugs, significantly relieved pain in children hospitalized because of pain from sickle cell disease. Credit: Robert Boston/School of Medicine

Many children with sickle cell disease experience frequent and severe pain episodes, requiring emergency room visits or hospitalization. In search of more effective ways to treat such pain, researchers at Washington University School of Medicine in St. Louis have found that adding a low dose of the drug methadone to standard treatment can limit pain experienced by children with the condition.

The study is available online in the journal *Pediatric Blood & Cancer*.

"More than half of sickle cell patients have at least one episode of significant pain every year, and about 20 percent experience multiple episodes each year that require hospital stays," said first author Jennifer Horst, MD, an instructor of pediatrics at the School of Medicine and an emergency room physician at St. Louis Children's Hospital. "In this study, the pediatric patients who received a one-time dose of methadone rated their pain levels much lower than those who took standard pain-killing drugs. In many cases, their pain went away, so we believe methadone has the potential to make life better for these pediatric patients."

The researchers followed 24 children and 23 adults who were hospitalized after suffering episodes of severe sickle cell pain.

Patients are treated with pain-killing drugs, usually opioids such as morphine, until their pain is under control. In this study, the researchers gave half of the patients a single, low dose of the long-duration opioid methadone. The result was that many of them then needed lower amounts than usual of other opioid drugs to control their pain.

Severe pain occurs when the shape of red blood cells becomes sickle-like in shape, making it more difficult for the cells to flow through blood vessels. As a result, the red blood cells don't supply enough oxygen to tissues in the body that need it.

Horst and senior investigator Evan D. Kharasch, MD, PhD, the Russell D. and Mary B. Shelden Professor of Anesthesiology, compared pain relief in patients given morphine with pain relief in those whose treatments were supplemented with methadone.

Morphine is the standard painkiller prescribed to sickle cell patients. Methadone also frequently is used to treat pain, particularly in patients having surgery or those with cancer. The latter drug also is used in detoxification and maintenance therapy for individuals who are dependent on opioid drugs, including heroin.

Study patients who did not receive methadone were given morphine to treat their pain. All of the patients in the study were able to regulate the amount of pain-killing drugs they received.

The children who received methadone rated their pain lower on a standard scale that indicated no pain to severe pain. They also rated their pain relief as better, at 7 to 8 on a scale of 1 to 10, while those who didn't get methadone rated their pain relief at around 4 or 5 during the first 72 hours of their hospital stays.

In adults, however, pain relief linked to methadone was not statistically significant. Kharasch—also a professor of biochemistry and molecular biophysics and director of the Center for Clinical Pharmacology, a research center operated by St. Louis College of Pharmacy and the School of Medicine—said the problem in adults may have been that their doses were too low.

"Because adult patients have lived with sickle cell disease their entire lives, it's possible they develop a tolerance to pain medications, and pain-killing drugs, including methadone, become generally less effective," he said. "However, we wanted to make sure methadone was safe to use in sickle cell patients, so we actually gave very low doses of the drug. That

might be why the adults didn't register the same improvements in pain scores."

Kharasch and Horst said methadone may help relieve pain from sickle cell disease because the drug has pain-killing properties that are different from morphine and because it remains in the body longer.

"Methadone has a faster onset and lasts longer than other, typical pain medicines, so we think it may be useful in getting some patients relief before they have to be hospitalized," Horst said. "We'd like to treat pain more quickly, especially in children, so that their pain crises can be resolved more quickly and they can go home sooner. Children who come in several times a year can miss a lot of school. That affects their quality of life."

More information: Jennifer Horst et al. Pharmacokinetics and analgesic effects of methadone in children and adults with sickle cell disease, *Pediatric Blood & Cancer* (2016). DOI: 10.1002/pbc.26207

Provided by Washington University School of Medicine in St. Louis