Study affirms challenges in managing severe pain of sickle cell disease

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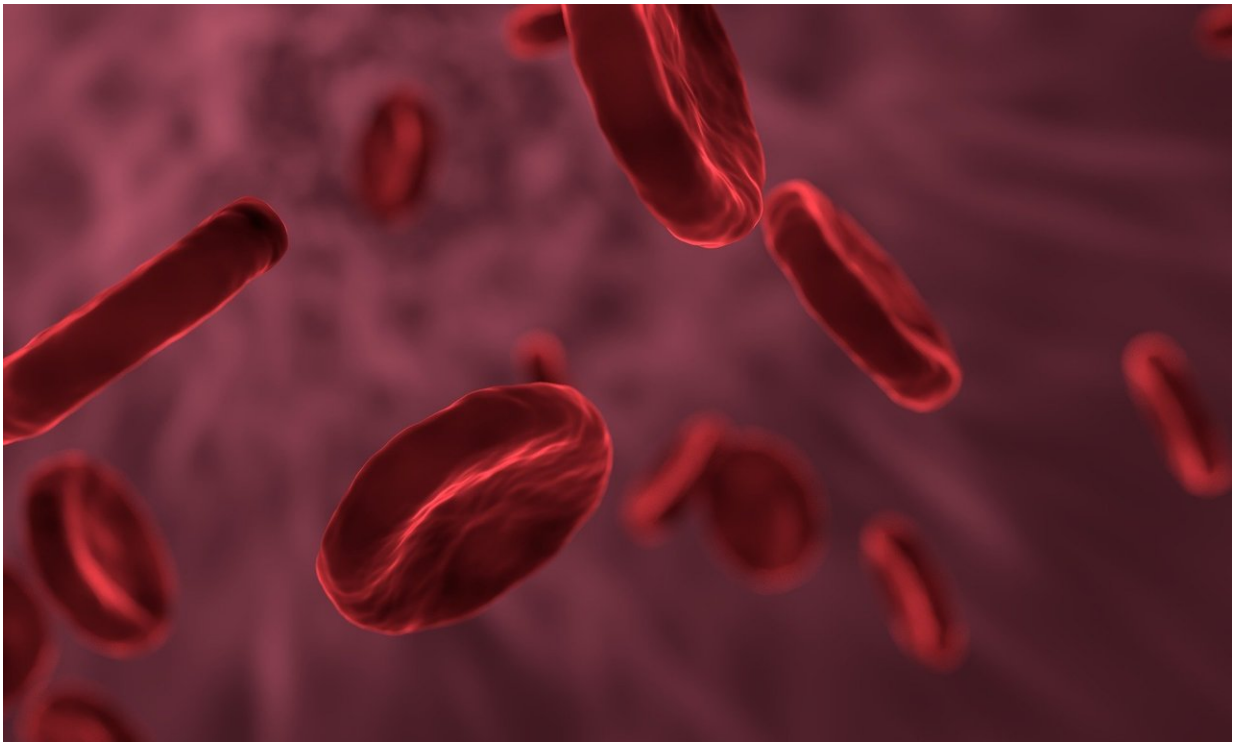

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In a study tracking the severe crisis pain of sickle cell disease and its management in 73 adults over a period of a year, Johns Hopkins researchers found that even among those on high doses of daily at-home opioids, a persistent subset was more likely to seek emergency hospital care for crisis pain and was less likely to have the pain controlled by

intensive treatment.

The researchers say their findings, described in the September issue of the *American Journal of Hematology*, underscore the persistent difficulties, poor patient outcomes and high costs associated with assessing and addressing the 10 to 20 percent of patients with sickle cell who are the sickest and have the most pain.

"Although progress has been made in managing the pain crises of many with sickle cell, there remains a group of sicker patients who seek hospital care with greater than typical frequency and whose pain is not being treated effectively," says C. Patrick Carroll, M.D., director of psychiatric services for the Johns Hopkins Sickle Cell Center for Adults and assistant professor of psychiatry and behavioral sciences at the Johns Hopkins University School of Medicine. "We want to focus our efforts on figuring out how to deliver high value care to our sickest patients."

Sickle cell disease is the most common inherited blood disorder diagnosed in the United States, affecting an estimated 100,000 people, most of them African-Americans. In addition, about one in 13 Americans of African descent carry one copy of the gene that causes sickle cell disease, and have "sickle cell trait." People who inherit two copies have sickle cell anemia, the disorder's most common form. The disorder is marked by the characteristic "sickled" or crescent-shape red blood cells that can get stuck in small blood vessels feeding bones, creating recurrent bouts of crippling pain that require opioids and sometimes urgent hospitalization. Beyond the disabling toll on patients, the disease accounts for a significant amount of health care costs—an estimated $500 million per year. About 10-20 percent of people with sickle cell account for more than 50 percent of the costs, Carroll says, reflecting the reality of patients with sickle cell whose pain episodes are more frequent and more intense than usual.

"The most clinically interesting finding but also the most puzzling was the extent to which higher opioid doses—both at home and during acute visits—were tied to poorer outcomes and more complications," says Carroll. "There is the conundrum that despite more aggressive treatment, a subset of people didn't get as much benefit."

He says growing tolerance to opioids may be one explanation, along with emergency room physicians who don't know a patient's history to quickly provide adequate pain medicines when pain crises occur, which may require higher opioid doses than are safe for a typical patient. Care is fragmented, Carroll says, and because there are no objective measures of pain, some physicians are reluctant to prescribe higher doses of opioids.

In their study that documented the source of higher-than-typical infusion center visits, the researchers looked at data from 73 patients seen at the Johns Hopkins Sickle Cell Center for Adults. Patients were an average age of 34, and 62 percent were women. Participants all underwent assessment on a standard Pain Anxiety Symptoms Scale, and researchers collected information on patients' socioeconomic status, insurance coverage and education level. The researchers relied on medical records to document admission to the Sickle Cell Infusion Center, where patients get treated for crisis pain. Opioid doses were converted to a standard measurement of "morphine equivalents" so drug quantity could be easily compared among participants.

With those data, the researchers classified 23 people as "typical" users of the infusion center (less than five visits over a year). Another 23 people were considered "high" users of the infusion center (five visits or more). The remaining 27 people had no visits in a calendar year.

Typical users of the infusion center were on an average of about 26 morphine equivalents of opioids daily at home, compared to high-users

who were on about 66 morphine equivalents of opioid medication daily.

Although the typical users had on average the same initial crisis pain rating as the high-users (8.5 versus 8.4 on a scale of 10), the typical users of infusion center care reported an average reduction of 3.8 pain points after treatment with opioids intravenously, putting their pain level around 5, compared to the high-users of infusion center care who only reported a drop of an average of 1.6 pain points, putting them at around 7 for reported pain after treatment. Pain improvement was twice as great for typical infusion center users, yet they received less than half the opioid dosage (~26 milligrams) during the emergency visits than those high users of the infusion center (~66 milligrams).

Because it's a challenge to manage pain effectively without prescribing potentially unsafe amounts of opioids, what's clear, Carroll says, is the need to develop more nonopioid pain relievers that don't increase risks of tolerance and overdose.

One of the biggest drivers of cost and ineffective treatment of people with sickle cell, he says, is that in many cases the health care team dealing with people in an emergency setting during crisis isn't the same providers who help the patient manage day-to-day care. "This typically means that emergency care providers don't reliably know medication dosages and treatment plans in place for that person," Carroll says.

There is a great need, he adds, for sickle cell disease clinical centers that manage both day-to-day and 24/7 emergency care, such as those with the integrated approach used by the Johns Hopkins Sickle Cell Infusion Center that can help bridge the care gap and keep treatment consistent.

Sickle cell disease is most common in people with ancestry near the equator, such as African, Indian, Asian, Middle Eastern and Mediterranean, or places where malaria is common. Sickle cell disease

can damage the internal organs and, on average, the life spans of people with the disease are 30 years shorter than in the general population.

More information: C. Patrick Carroll et al. Predictors of acute care utilization and acute pain treatment outcomes in adults with sickle cell disease: The role of non-hematologic characteristics and baseline chronic opioid dose, *American Journal of Hematology* (2018). DOI: 10.1002/ajh.25168

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