Researchers study effect of chronic opioid therapy on pain and survival in sickle cell disease

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New UMN research recently published *Blood Advances*, Kalpna Gupta, Ph.D., Professor of Medicine, University of Minnesota Medical School, demonstrates the impact of opioids on the survival of humanized mouse models with sickle cell disease, compared to normal mice.

Sickle Cell Disease (SCD) affects millions of people throughout the world. The genetic disease worsens over time and can cause lifelong pain . Given the often severe nature of the pain associated with SCD opioid use is a rule not an exception for treatment. The mice in this study showed characteristics of pain observed in patients with Sickle Cell Disease (SCD).

"We wanted to know if opioids reduce survival," said Gupta. "There was a distinct difference in survival with morphine treatment between control mice expressing normal human hemoglobin and sickle mice expressing human sickle hemoglobin." Gupta and her colleagues found that chronic morphine treatment decreased survival in control mice, but not in sickle mice.

Adverse effects of opioids from clinical studies in cancer show the association of opioid requirement with reduced survival. Patients with SCD have reduced survival. Since many use opioids long-term, it is critical to know if opioids reduce survival in SCD and if they are really required. Researchers also looked into whether opioids caused

hyperalgesia, a condition where a person develops an increased sensitivity to pain. They found that chronic morphine treatment leads to hyperalgesia in sickle mice, but does not lead to analgesic tolerance.

"Our findings show that opioids cause hyperalgesia, which means they do cause pain, and that is why there is an increased requirement of morphine as the time goes by, it may not due to the reward function." This study provides evidence for the first time that opioid requirement in SCD may be genuine and is not causing an adverse effect on survival and that even after long-term use opioids continue to remain effective in treating pain.

According to Gupta, it would be critical to perform observational analysis on SCD patients receiving opioids to validate these findings, so that their pain can be managed effectively without opioidphobia amongst the providers. Until alternatives to opioids are found, pain needs to be treated with opioids. However, this study in humanized sickle mice also highlights the unmet need to develop effective analgesics to treat pain in SCD and in many other conditions.

Provided by University of Minnesota

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