A safer, more effective morphine may be possible with IU discovery

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An orphan drug originally used for HIV treatment has been found to short-circuit the process that results in additional sensitivity and pain from opioid use. The study by researchers at the Indiana University School of Medicine is reported in the March 25, 2011 issue of *Brain, Behavior and Immunity.*

The researchers say the finding in animal models may ultimately make morphine a safer and more effective drug.

Traditionally opioids were used to relieve pain following surgery, from cancer and at the end of life. Today opioids are used widely for chronically painful conditions like osteoarthritis and back pain and may need to be prescribed for decades.

Morphine, the gold standard for controlling moderate to severe pain, has debilitating side effects including reduced respiration, constipation, itching and addiction. Patients also develop a tolerance to morphine which can lead to a complicated spiral.

"In addition to the recognized side effects, morphine actually creates sensitivity and causes more pain through inducing an inflammatory response in the body," said first author Natalie Wilson, a National Science Foundation Fellow at the IU School of Medicine.

This increased sensitivity is clinically known as opioid-induced hyperalgesia (OIH). Frequently, patients receiving opioids for pain

control may actually become more sensitive to certain painful stimuli necessitating an increased opioid dosage. OIH may also represent one of many reasons for declining levels of analgesia while receiving opioids or a worsening pain syndrome.

"The drug itself is producing its own new pain," said Fletcher A. White, Ph.D., Vergil K. Stoelting Professor of Anesthesia and director of Anesthesia Research at the IU School of Medicine. "I tend to view it as an injury as it appears to be creating another pain."

Dr. White explained that morphine sets into motion a cascade of events, one of which is to increase molecular communication to and from the nerves by a protein known as CXCR4. This increase in CXCR4 signaling contributes to a neuroinflammatory response causing increased sensitivity and additional pain.

Drs. Wilson and White and colleagues administered AMD3100, an orphan drug known to block the CXCR4 response, to rats. By halting the signaling process, the researchers interrupted the OIH response, Dr. White explained. "If this translates appropriately in people, this application would likely make morphine a safer, more effective drug for chronic pain control."

Provided by Indiana University School of Medicine