New medication more potent, longer lasting than morphine

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(PhysOrg.com) -- A little-known morphinelike drug is potentially more potent, longer lasting and less likely to cause constipation than standard morphine, a study led by a Loyola University Health System anesthesiologist has found.

The drug, morphine-6-0-sulfate, has a similar chemical structure to standard morphine. Dr. Joseph Holtman Jr. and colleagues reported that a study they performed in rats "demonstrated potential clinical advantages of morphine-6-0-sulfate compared to morphine."

Holtman is first author of the study, published in the December 2010 issue of the *European Journal of Pharmacology*.

Holtman is medical director of Loyola's Pain Specialty Service and a professor in the departments of Anesthesiology and Molecular Pharmacology and Therapeutics of Loyola University Chicago Stritch School of Medicine. He directed the study while he was at the University of Kentucky's College of Medicine. He joined Loyola on March 1, 2010.

Opioids, such as morphine, oxycodone and hydrocodone, are standard drugs for treating moderate to severe pain, including cancer pain. But these drugs can have significant side effects, including constipation, nausea, vomiting, drowsiness, cognitive dysfunction and slowed breathing and heart rates. And while opioids work well for conditions such as back pain and post-operative pain, the drugs are less effective against neuropathic pain, such as tingling, burning or shooting pain.

Constipation is a common side effect of morphine and can be so uncomfortable that some patients limit their use of the drug. Doctors typically do not discharge surgery patients until they have had a bowel movement and this can extend hospital stays.

Holtman and colleagues tested standard morphine and morphine-6-0-sulfate on rats. The animals received the drugs three ways -- by mouth, by IV and by injection into the space surrounding the spinal cord.

The rats underwent several well-established tests to determine their sensitivity to pain. In one such test, researchers focused a very warm light beam on the tail and measured how long it took for the rat to flick the tail.

In this tail-flick test, morphine-6-0-sulfate was 10 times more potent than standard morphine when administered in the space surrounding the spinal cord, five times more potent when administered by IV and two times more potent when given by mouth. Morphine-6-0-sulfate maintained its maximum effect for three hours, compared with 1½ hours for standard morphine. And it took rats 25 days to build tolerance to morphine-6-0-sulfate, compared with 10 days with standard morphine.

Morphine-6-0-sulfate also was more potent than standard morphine for neuropathic and inflammatory pain.

Researchers found that morphine-6-0-sulfate could cause constipation, but only at doses 10 to 20 times higher than the effective doses.

The findings suggest that morphine-6-0-sulfate "may be an interesting potential drug for further study," Holtman and colleagues wrote.