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More Evidence of the Power of Mesenchymal Stem Cell Transplant to Block Opioid-Induced Hyperalgesia and Tolerance

Feb. 18, 2016, PALM SPRINGS, Calif. – Cleveland Clinic researchers have found new evidence that modulating neuroinflammation with stem cell transplants may prove to be an effective strategy to treat both opioid tolerance (OT) and opioid-induced hyperalgesia (OIH). The latest results in this line of inquiry, which may have the potential to transform opioid therapy for pain, are on view today at the 32nd Annual Meeting of the American Academy of Pain Medicine.

The investigators found that the development of OT and OIH was effectively prevented in rats by either intravenous (IV) or intrathecal mesenchymal stem cell (MSCs), which were transplanted before morphine treatment. Furthermore, established OT and OIH were significantly reversed when the timing of the transplants followed repeated morphine injections.

"We have demonstrated that MSC transplantation promises to be a potentially safe and effective way to prevent and reverse two of the major problems associated with opioid therapy," said Jianguo Cheng, MD, PhD, professor of anesthesiology and director of the Cleveland Clinic Pain Medicine Fellowship Program.

"This emerging therapy has enormous potential to profoundly impact clinical practice. It may improve the efficacy of opioid therapy, reduce the risk of opioid overdose and save lives," he said.

Neuroinflammation that involves activation of microglia and astrocytes in the central nervous system contributes greatly to OT and OIH. Both OT, in which higher doses become necessary, and OIH, a heightened pain response, can limit effectiveness and compromise safety during opioid therapy to treat pain. The anti-inflammatory and immune modulatory properties of MSCs have been previously demonstrated. Last year, the same scientific research team reported that intrathecal MSC transplant reduced OIH and OT in rats. For the current study, the investigators further tested the anti-tolerance and anti-hyperalgesia effects of MSC, this time by IV application and in mice as well as rats.

The IV transplant was given seven days before or 14 days after the initiation of daily morphine injections to test both the preventive and therapeutic effects of MSCs. Investigators evaluated OT and OIH by foot withdrawal thresholds in response to mechanical or thermal stimulation. They

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also examined multiple safety parameters, including normal locomotion, body weight gain, liver and kidney function, and vital organ pathology exams.

Using immunohistochemistry, they found that the treatments significantly reduced the activity of microglia and astrocytes in the spinal cord. The analysis of safety measures revealed no abnormalities in the animals' vital organs or functions. The investigators are planning a preclinical investigation in preparation for clinical trials.

Poster 233 – Intravenous Transplantation of Bone Marrow–Derived Mesenchymal Stem Cells Attenuated Activation of Glial Cells and Reversed Opioid Tolerance and Opioid-Induced Hyperalgesia
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The American Academy of Pain Medicine is the premier medical association for pain physicians and their treatment teams with some 2,400 members. Now in its 33rd year of service, the Academy's mission is to optimize the health of patients in pain and eliminate pain as a major public health problem by advancing the practice and specialty of pain medicine through education, training, advocacy and research. Information is available on the Academy's website at www.painmed.org.

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