Stem cell injections improve diabetic neuropathy in animal models

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Diabetic neuropathy (DN) is a condition in which perpetually high blood sugar causes nerve damage, resulting in a myriad of symptoms such as numbness, reduced ability to detect painful stimuli, muscle weakness, pain, and muscle spasms. DN affects up to 60 percent of patients with diabetes, is often the cause of foot ulcers, and can ultimately result in amputations. There is no curative therapy for DN, but a recent study carried out by a team of researchers in the U.S. and Korea has found that laboratory animals modeled with DN can experience both angiogenesis (blood vessel growth) and nerve re-myelination following injections of mesenchymal stem cells derived from bone marrow (BM-MSCs).

Their study will be published in a future issue of *Cell Transplantation* and is currently freely available on-line as an unedited early e-pub.

The researchers used mesenchymal stem cells, which can be easily isolated from a variety of sources, such as adipose (fat) tissues, tendons, peripheral blood, umbilical cord blood, and bone marrow. MSCs derived from bone marrow (BM-MSCs) have been among the most successfully transplanted cells, offering therapeutic benefits for a wide range of conditions, from serious burns to cardiovascular diseases, including heart attack and stroke.

In this study, laboratory rats modeled with diabetes were randomly assigned to BM-MSC or saline injection groups 12 weeks after the induction of diabetes. The non-diabetic control group of rats was age- and sex-matched. DN was confirmed by latency in nerve conduction

velocity tests.

"We investigated whether local transplantation of BM-MSCs could attenuate or reverse experimental DN by modulating angiogenesis and restoring myelin, the electrically insulating substance surrounding nerves that is reduced by DN," said study co-author Dr. Young-sup Yoon, Professor at the Department of Medicine, Division of Cardiology at Emory University School of Medicine. "In this study we have provided the first evidence that intramuscular injected BM-MSCs migrate to nerves and can play a therapeutic role."

According to the researchers, their findings indicate that intramuscular injection of MSCs resulted in an increase of multiple angiogenic and neurotrophic factors associated with blood vessel growth and subsequently aided the survival of diabetic nerves, suggesting that BM-MSC transplantation restored both the myelin sheath and nerve cells in diabetic sciatic nerves.

"We identified several new mechanisms by which MSCs can improve DN," said the researchers. "First, we demonstrated that numerous engraftments migrated to and survived in the diabetic nerves. Second, we demonstrated a robust increase in vascularity. Third, we found the first evidence that MSCs can directly modulate re-myelination and axonal regeneration."

The researchers concluded that DN, for which there is no other therapeutic option, can be an "initial target for cell therapy" and that transplantation of BM- MSCs "represents a novel therapeutic option for treating DN."

"Currently, the only treatment options available for DN are palliative (focused on alleviating pain) in nature, or are directed at slowing the progression of the disease by tightly controlling blood sugar levels, "says

Dr. John R. Sladek, Jr., Professor of Neurology, Pediatrics, and Neuroscience, Department of Neurology at the University of Colorado School of Medicine. "This study offers new insight into the benefits of cell therapy as a possible treatment option for a disease that significantly diminishes quality of life for diabetic patients. Safety and efficacy for human application must be evaluated to further determine the feasibility of BM-MSC transplantation for treatment of DN."

More information: Han, J. W.; Choi, D.; Lee, M. Y.; Huh, Y. H.; Yoon, Y-S. Bone marrow-derived mesenchymal stem cells improve diabetic neuropathy by direct modulation of both angiogenesis and myelination in peripheral nerves. *Cell Transplant.* Appeared or available on-line: May 13, 2015. http://ingentaconnect.com/content/cog/ct/pre-prints/content-CT-1386_Han_et_al

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