

Cell Transplantation reports a success in treating end-stage liver disease

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Transplanting their own (autologous) bone marrow-derived stem cells into 48 patients with end-stage liver disease resulted in therapeutic benefit to a high number of the patients, report researchers publishing in the current issue of *Cell Transplantation* (19:11). Yet, the mechanism by which the infusion of CD34+ stem cells improves liver function remains elusive, they say.

The study, carried out by a team of researchers in California and in Egypt, is now freely available on-line at <http://www.ingentaconnect.com/content/cog/ct/>.

According to the study's corresponding author, Dr. Mark A. Zern of the University of California Davis Medical Center, Sacramento, CA, patients with end-stage liver failure in Egypt have few treatment options but for transplantation. A shortage of donors and cost factors make that strategy unrealistic. Accordingly, this study sought to evaluate the safety and efficacy of transplanting autologous bone marrow-derived CD34+ [stem cells](#) in 48 patients, 36 of whom had chronic, end-stage hepatitis C-induced liver disease, and 12 with end-stage autoimmune liver disease.

"For all patients there was a statistically significant decrease in peritoneal cavity fluid, or 'ascites,'" said Dr. Zern. "There was also clinical and biochemical improvement in a large percentage of patients who received the transplantation."

The researchers reported that they obtained "reasonable numbers of

CD34+ cells" that were then "amplified and partially differentiated into hepatocyte [precursor cells](#)."

"This enabled us to transplant as many as one billion of these cells per patient," explained Dr. Zern. "The finding of improvement in ascites in a significant number of patients is impressive and somewhat surprising, suggesting that [cell transplantation](#) might be clinically significant beyond the improvement in laboratory parameters."

They also report using granulocyte-colony stimulating factor (G-CSF) to "mobilize...CD34+ stem cells into peripheral circulation." The researchers anticipated that G-CSF would likely enhance a variety of circulating bone marrow-derived cells, producing growth factors which could "positively affect liver regeneration and perhaps have a positive effect on portal hypertension."

The team also reported that prior to transplantation, the cells were already beginning to develop a hepatocyte phenotype while in culture, suggesting that the cells may have acted as hepatocyte-like cells following engraftment. The researchers plan to compare routes of infusion to determine if peripheral infusion of transplanted cells will be adequate.

"The use of peripheral infusion would dramatically reduce both costs and risks for this cell transplantation, thus making the treatment an even more viable option in Egypt and throughout the world," concluded Dr. Zern.

"It would be very interesting to determine if the differentiation to hepatic precursors was a necessary step for this treatment," said Dr. Stephen Strom, a professor of pathology in the Department of Pathology at the University of Pittsburgh and section editor for *Cell Transplantation*. "Other research groups are now showing similar results

with cells without any hepatic characteristics, including fractionated and unfractionated bone marrow and mesenchymal stem cells. Taken together, these data suggest that the positive effects these researchers find may be the result of paracrine effects from factors secreted by the donor cells. I look forward to reading about the outcome of future studies to determine the optimal route of administration and dose of these cells, as well as more long term follow up."

More information: Salama, H.; Zekri, A-R.; Zern, M.; Bahnassy, A.; Loutfy, S.; Shalaby, S.; Vigen, C.; Burke, W.; Mostafa, M.; Medhat, E.; Alfi, O.; Huttinger, E. Autologous Hematopoietic Stem Cell Transplantation in 48 Patients With End-Stage Chronic Liver Diseases. *Cell Transplant*. 19(11):1475-1486; 2010

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