Medscape

Combination Stem-Cell Transplant May Benefit Type 1 Diabetes

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December 08, 2015

VANCOUVER, British Columbia — Transplantation of cells from umbilical cords along with autologous bone-marrow stem cells may represent a promising new approach for treating patients with established type 1 diabetes, a new proof-of-concept study suggests.

One-year findings from an open-label randomized trial of 42 patients who received either the combined transplanted cells or standard care were presented December 1 here at the World Diabetes Congress 2015 by Xiumin Xu, director of China-USA Collaborative Human Cell Transplant Program at the Diabetes Research Institute at the University of Miami, Coral Gables, Florida, and were simultaneously published in Diabetes Care.

Ms Xu noted that therapeutic strategies for type 1 diabetes must address the autoreactive host immune system as well as pancreatic beta-cell repair and regeneration.

Most type 1 diabetes clinical trials have been conducted in patients soon after disease onset, but increasing evidence suggests that some level of insulin production is maintained in many patients even years after diagnosis, she added.

Session moderator and Diabetes Care editor William T Cefalu, MD, executive director, Pennington Biomedical Research Center, Louisiana State University, Baton Rouge, told Medscape Medical News, "This paper showed that interventions may show an effect even after many years of having established type 1 diabetes....The authors showed, at least in this study, there was some improvement in endogenous C-peptide, insulin levels, HbA1c, and fasting glucose."

Glycemic Parameters Improved With Combination Transplant

In the study, the researchers used mesenchymal stromal cells extracted from umbilical cords; these cells are considered multipotent stem cells and can also be isolated from bone marrow, adipose tissue, and placenta, among other tissues, and have been shown to modulate immune responses and tissue repair, Ms Xu explained.

But previous work has suggested that mesenchymal stromal cells alone might not be sufficient for the type of tissue regeneration and repair needed. So the scientists used autologous bone-marrow mononuclear cells in addition.

Both types of cells induce regeneration of recipient-derived pancreatic insulin-secreting cells, while the mesenchymal cells inhibit T-cell–mediated responses against the newly formed beta cells.

Study participants were aged 18 to 40 years, had been diagnosed with type 1 diabetes for longer than 2 years but less than 16 years, had HbA1c levels of 7.5% to 10.5%, and had daily insulin requirements of less than 100 units.

To ensure homogeneity, umbilical-cord mesenchymal stromal cells used in the trial were all obtained from a single human donor umbilical cord. The autologous bone-marrow mononuclear cells were aspirated from both iliac crests of the participants under local anesthesia.

Patients were fasted and received prophylactic octreotide prior to the transplantation procedure. Catheterization was performed under angiographic guidance. The dorsal pancreatic artery was identified, and 60 to 80 mL of the bone-marrow cells were infused, followed by 30 to 50 mL of the umbilical-cord mesenchymal stromal cells.

At 1 year, the primary end point, C-peptide secretion, increased significantly in the stem-cell–transplant group, with 15 of 21 (71%) showing increased levels (P = .00012). In contrast, C-peptide decreased by 7.7% among the 21 controls (P = .013 vs transplant group).

Insulin levels increased in the stem-cell–transplant group by 49% (P = .01) while decreasing by 5.7% in the control group (P = 0.27 vs transplant).

HbA1c levels dropped significantly at 3, 6, 9, and 12 months in the cell-transplant patients, while remaining stable in the control group (P < .01 at all time points). The decline was from 8.6% to 7.5% with the transplanted cells, in contrast to a rise from 8.7% to 8.8% for the controls.

Similarly, significant reductions were seen among the cell-transplant patients in fasting blood glucose levels.

And although insulin independence was not achieved, insulin requirements were reduced by 29.2% with the cell transplant (P = .001), while remaining unchanged in the controls.

Cell Treatment Well Tolerated

At 12 months, patients in the transplanted group showed decreased anxiety and depression symptoms and improved quality-of-life scores, whereas these measures didn't change significantly in the control group.

Patient-reported severe hypoglycemic events were also lower in the stem-cell–transplant vs control group (P = 0.02).

No significant changes were seen in C-reactive protein, white blood cell counts, hemoglobin, serum creatinine, or alanine aminotransferase. No severe adverse events, such as malignant tumors, were observed during the follow-up period.

Overall glutamic acid decarboxylase antibody-positive rates at 1 year were not significantly different between the two groups (57% in stem-cell–transplant group and 52% in controls).

Dr Cefalu commented: "It was a small study, but the fact that they were able to do this and show some benefit, particularly in those with type 1 diabetes for a little longer, was a step forward. More longer-term and larger studies will be needed at this time in order to fully evaluate the intervention as to efficacy."

This study was supported by the Fujian Province, the People's Liberation Army Clinical Innovation Major Project Fund, and the Natural Science Foundation of Fujian Province. Generous support by the Diabetes Research Institute Foundation is acknowledged. Ms Xu and the other study authors have no further relevant financial relationships. Dr Cefalu is a consultant for Intarcia Therapeutics and Sanofi and has been a principal investigator of studies for GlaxoSmithKline, AstraZeneca, and Janssen.

Diabetes Care. Published online December 1, 2015. Article