Fetal Pancreatic Stem-Cell Transplant in Patients With Diabetes Mellitus

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Abstract

Objectives: To determine the efficacy of fetal stem cell transplant for treating patients with diabetes mellitus types 1 and 2.

Materials and Methods: Five patients with diabetes mellitus type 1 and 5 patients with diabetes mellitus type 2 (aged 18-56 years) received a fetal pancreatic stem-cell transplant (cells were 16-18 wk gestation) performed by intravenous infusion at 50 mL/hour. The quantity of fetal stem cells infused was $\geq 5.8 \times 10^6$. We analyzed the patients’ C-peptide and glycated hemoglobin levels both before and 3 months after fetal stem cell transplant.

Results: In patients with diabetes mellitus type 1, fetal stem-cell transplant led to a significant increase in C-peptide levels, from 0.09 ± 0.01 ng/mL to 0.20 ± 0.07 ng/mL, after 3 months ($P < .008$).

Conclusions: Treatment with fetal pancreatic stem cells may be beneficial for treating patients with type 1 or type 2 diabetes.

Key words: C-peptide, Glycated hemoglobin, Pancreatic islet-cell regeneration

Introduction

The prevalence of diabetes mellitus (DM) is increasing rapidly in industrialized countries, where it has reached a prevalence of 5% to 6%, as well as in the developing countries, which ranks first in prevalence among endocrine and metabolic diseases.1-4 According to an International Diabetes Federation (IDF) report from 2014, a total of 387 million people worldwide had DM; each year, the number of patients has increased by 5% to 7%, and every 12 to 15 years, it has doubled.5 The IDF forecast indicates that by 2035, the number of people with diabetes will reach 592 million.5 Further, according to research conducted by M.E. Zeltzer in Kazakhstan, the true prevalence of the disease is 2 to 5 times higher than the officially recorded level.6,7

The long-term survival and performance capabilities of patients with DM type 1 are enhanced by lifelong insulin replacement therapy. Significant advances have been made in the production of various medical insulin products (eg, monocomponent genetically engineered short-acting and medium-acting human insulin medications, short-acting and long-acting human insulin analogues) and means of administration (eg, insulin syringes, pens, and pumps for continuous infusion of insulin). However, numerous problems persist in clinical practice around the inability to achieve full compensation in diabetes, ie, the normalization of carbohydrate metabolism for an extended period. Normalization of carbohydrate metabolism is indispensable to preventing the microvascular and macrovascular complications of diabetes, which are known to cause early disability and raise the patients’ mortality rate.8

Since the second half of the 20th century, numerous studies have been done to define a mechanism for replacing the lost function of the islets of Langerhans, to restore functioning to the pancreas’s insular apparatus, and to normalize carbohydrate metabolism regulation. During this era, international protocols (eg, the Edmonton Protocol of 2000) were developed and implemented, as were national registries of pancreatic tissue for transplant.9,10
Both type 1 and type 2 diabetes are characterized by a deficit in pancreatic beta cell mass. Thus, stem cells obtained from the pancreatic tissue of fetuses represent a potentially effective approach to regenerating islet cells. One modern therapeutic approach to this problem is fetal stem-cell transplant (FSCT).

Materials and Methods

This case study included 10 individuals: 5 patients with DM type 1 and 5 patients with DM type 2, aged 18 to 56 years (mean age: 36.2 ± 13.3 y). Fetal pancreatic stem cells were extracted from the pancreatic tissue of an aborted fetus at 16-18 weeks’ gestation. Then FSCT was performed using intravenous infusion at a rate of 50 mL/hour. The quantity of fetal stem cells infused was ≥ 5-8*10⁶.

Both before and 3 months after FSCT, C-peptide and glycated hemoglobin (HbA1c) were analyzed. This clinical study and its methods were approved by the Ethics Committee at our institution.

Statistical analyses were performed using standard methods and Statistica version 6.0 software (StatSoft Inc., Tulsa, OK, USA). Clinical assessments of patients, as described, were calculated using averages, margin of error, and standard deviation. To compare independent groups, we used the nonparametric Mann-Whitney U test.

Results

Before FSCT, all patients with DM type 1 and DM type 2 had poor glycemic control. Among all patients, HbA1c was > 7%; in patients with type 1 DM, it averaged 9.52 ± 1.96%, and in patients with type 2 DM, it averaged 8.86% ± 3.23% (Table 1).

Before FSCT, all patients with type 1 DM had a mean level of C-peptide 0.09 ± 0.01 ng/mL, below the established norm. The mean level of C-peptide in patients with type 2 DM was 2.24 ± 0.84 ng/mL, within the normal range (Table 1).

On the day of FSCT, patients with DM type 1 continued to receive intensified insulin therapy; patients with DM type 2 were given hypoglycemic agents in the form of tablets or insulin subcutaneously. The dosage was adjusted according to the metabolism performance level, which was examined once every 3 hours during the first day of FSCT. During the subsequent 3 days, fasting glucose

Discussion

The tendency of C-peptide to increase after FSCT in patients with DM type 1 and type 2 in our study demonstrated the effectiveness of FSCT. This result indicates that FSCT was successful in helping to end insulin dependence, which is vitally important especially for patients with DM type 1.10

Three months after FSCT, HbA1c levels decreased in patients with DM types 1 and 2. We assume that the lack of a statistically significant reduction in HbA1c in our study probably resulted from the slower decline in C-peptide in the absence of immunosuppressive therapy, which is usually administered during islet cell transplant.10 Similar results were achieved in a study by Bretzel and associates,11 who also did not administer immunosuppressive therapy to their stem cell transplant patients with DM.

Based on our study results, treatment with fetal pancreatic stem cells may be beneficial in DM type 1 and type 2. Further studies with a larger number of patients would help to confirm these findings and to achieve more robust results.
References