

American Transplant Congress, Philadelphia 2020

Beta Cell Replacement Therapy In Nonuremic Patients With Brittle T1DM Allows For Durable Long Term Insulin Independence Halting Progression Of Secondary Diabetic Complications

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Purpose: Beta cell replacement therapy in form of pancreas or islet transplantation is the only effective treatment for patients suffering from hypoglycemic unawareness despite intensive insulin treatment. Transplant provide endogenous insulin allowing for physiologic optimal blood glucose control.

Methods: 13 consecutive nonuremic patients with “brittle” type 1 diabetes (T1DM) received 27 islet transplants (up to 3 islet infusions) and 4 of them subsequently pancreas transplantation to extend benefit of insulin independence. Thymoglobulin was used during first islet transplant and basiliximab prior to subsequent islet and pancreas transplants for induction, whereas tacrolimus and mycophenolate for maintenance immunosuppression. Patient received Reparixin, etarcept or no anti-inflammatory therapy in peritransplant period.

Results: Three patients developed DSA with antibody mediated rejection and 1 severe cytokine release syndrome and 1 bleeding, which compromised islet graft function. Overall 1, 2, 3 and 5 year insulin independence rate after first islet transplantation was 11/13 (85%), 11/13 (85%) and 8/13 (61%), 6/13 (46%), respectively. Four patients received pancreas tx after median 4.5 years (3.5-6.5) increasing 5 and 6 year insulin independence rate to 69% (9/13) and 70% (7/10), respectively. Currently, 10/13 77% (10/13) are still off insulin with median follow 6.5 (5-7.5). Remaining 2 patients dropped the study due to social reasons right after their first or second islet transplant, another one dropped due to leukemia. Secondary diabetic complications such as the diabetic neuropathy remained stable but retinopathy improved in 4/13 patients (30%). None of the patients experienced any of the cardiovascular events. One patient with creatinine 1.55 mg/ml (GFR = 59) received kidney together with pancreas transplantation.

Conclusion: Beta cell replacement therapy in form of islet and subsequent pancreas transplantation has proven its long term efficacy in restoring normoglycemia and alleviating the immediate burden of hypoglycemic unawareness as well as preventing progression of secondary complications.