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Stem cell therapies in diabetes mellitus

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Type 1 diabetes mellitus (T1DM) results from autoimmune destruction of insulin producing β-cells in the pancreas. The standard treatment for T1DM is insulin replacement and currently there is no curative therapy. Islet cell transplantation has been performed since the 1990s, but it has a number of disadvantages such as limited access to the procedure, shortage of cadaveric donors and immune rejection that ultimately leads to recurrence of the autoimmune pancreatic β-cell destruction. However, the Edmonton protocol of islet cell transplantation which excludes glucocorticoids from the immunosuppressive therapy has led to higher response rates and longer durations of insulin independence. Insulin-producing stem cells offer a potential solution to donor limitation. The use of certain types of stem cells in animal models and in early human clinical trials has shown remarkable results and promising success. The following types of stem cells have been utilized: mesenchymal stem cells (MSCs), induced pluripotent stem cells (iPSCs), embryonic stem cells (ESCs) in addition to hematopoietic stem cells (HSCs). Different sources of stem cells such as the bone marrow (BM), Wharton's jelly of the umbilical cord and adipose tissue with different routes of stem cell administration have been employed. Recently, several animal studies on the use of MSCs in the treatment of T1DM have been performed. The results obtained so far include reversal of hyperglycemia and glycosuria, reversal of glomerular hypertrophy and tubular dilatation in addition to improvement in survival and blood glucose levels. Two published clinical studies on the use of MSCs in the treatment of T1DM in humans that included 5 and 11 patients showed the following outcomes: Reduced insulin requirements, reduced blood levels of *HbA1C*, increased serum levels of C-peptide, abolition of diabetic ketoacidosis and avoidance of immunosuppression. Only one human randomized clinical study on MSC therapy for T1DM has been published. The study included 29 patients and MSCs were obtained from the umbilical cord Wharton's jelly. The study showed safety and effectiveness of the procedure, while restoration of the pancreatic β-cell function took a long period of time. In a single case report, combination of adipose tissue derived-MSCs and BM derived-HSCs resulted in a significant amelioration of the biochemical profile of complicated DM over a period of 27 months. iPSCs are relatively safe and they can be derived from the patient (an autologous source) or from a donor (an allogeneic source). In several mouse models, iPSCs have been used to generate β-like cells similar to endogenous insulin secreting pancreatic β-cells and their use resulted in long-term correction of hyperglycemia. In a single study, undifferentiated pluripotent cells obtained from a human embryo produced high proportions of insulin producing β-cells that were capable of secreting insulin in addition to expressing other β-cell markers. Stem cell therapies require quality control and specific protocols for their future use in humans. Their long-term adverse effects such as the risk of malignant transformation have to be taken seriously. Despite being in its early clinical phase and despite having few obstacles and potential complications, the use of stem cell therapies in the treatment of T1DM seems very promising and may bring cure to this common intractable disease in the near future.

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