Beneficial effects of parenteral GLP-1 delivery by cell therapy in insulin-deficient streptozotocin diabetic mice.

Abstract

Parenteral delivery of long-Acting glucagon-like peptide-1 (GLP-1) mimetics has received much attention as a therapeutic option for diabetes. However, cell therapy-based GLP-1 treatments may provide a more physiological regulation of blood glucose. The present study assessed the effects of chronic GLP-1 delivery by cell therapy, using the GLP-1-secreting GLUTag cell line, in normoglycemic and streptozotocin-induced diabetic mice. GLUTag cell aggregates were transplanted into the subscapular region of mice. Over 30 days, cellular transplantation gave rise to encapsulated and well-vascularized growths, which contained immunoreactive GLP-1. Cell implantation was well tolerated and had no appreciable metabolic effects in normal mice. However, transplantation significantly (P<0.001) countered excessive food and fluid intake in diabetic mice and maintained normal body weight. Circulating glucose (P<0.01) and glucagon (P<0.05) were significantly reduced and plasma insulin and GLP-1 dramatically increased. This was associated with significantly (P<0.01) improved glucose tolerance in diabetic mice. Histological examination of the pancreata of these mice revealed elevations (P<0.001) in islet and β-cell area, with reduced (P<0.001) -cell area. Increased β-cell mass reflected the enhanced proliferation relative to apoptosis. These studies emphasize the potential of chronic GLP-1 delivery by cell therapy as a potential therapeutic option for diabetes.

Keyword: Beta-cell; Diabetes; Glucagon-like peptide-1 (GLP-1); Glucose tolerance; Insulin secretion; Streptozotocin.