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.