Total Pancreatectomy With Islet Cell Transplantation for the Treatment of Pancreatic Cancer

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Resection or removal of the pancreas causes loss of parenchyma, which can result in extreme disruption of glucose homeostasis and malabsorption of dietary nutrients. However, islet autotransplantation (IAT) may reduce or prevent the severity of pancreatic cancer. This article explores total pancreatectomy with IAT within the context of pancreatic cancer treatment.

At a Glance
- The liver is the preferred site for implantation because of easy vascular access.
- Following islet autotransplantation, the liver becomes an insulin-producing organ as the transplanted beta cells begin making insulin.
- The most significant complication of implantation in the liver is portal vein occlusion because of thrombosis; consequently, a heparin drip is infused for the first seven days postoperatively to prevent portal vein thrombus formation.

The pancreas is an exocrine and endocrine digestive organ in the gastrointestinal tract. The exocrine function of the pancreas aids in digestion of carbohydrates, protein, and fat, whereas the endocrine or hormone-producing function assists in glucose homeostasis. Acini cells produce pancreatic enzymes and an aqueous solution. Three main pancreatic enzymes (amylase, trypsin, and pancreatic lipase) assist in carbohydrate, protein, and fat digestion. The aqueous solution functions to raise duodenal pH. This pH is neutralized by gastric acid, allowing increased pancreatic acid activity (Brendle, 2010).

The islets of Langerhans contain four main endocrine-producing cells: alpha, beta, delta, and F cells. Glucagon is manufactured in the alpha cells, and its function is to maintain normal blood glucose levels. This is accomplished by glycogenolysis and gluconeogenesis. Beta cells are involved in the metabolism of sugars, carbohydrates, proteins, and fats, and they produce insulin, which aids in cell uptake of glucose and assists in intracellular activity. Delta cells produce somatostatin that helps to regulate various hormones (e.g., thyroid-stimulating hormone, growth hormone, other gastrointestinal hormones). F cells produce pancreatic polypeptides that aid in gallbladder emptying.

Pancreatic resection or removal causes loss of parenchyma, leading to extreme disruption of glucose homeostasis (Balzano et al., 2013). This disruption is often called pancreaticogenic diabetes (PD) and is characterized by extreme hyperglycemia and hypoglycemia, increased morbidity and mortality, and target organ damage (i.e., nephropathy, neuropathy, and retinopathy) (Balzano et al., 2013). These patients rarely develop ketoacidosis, usually show mild hyperglycemia, and are very sensitive to insulin administration, with frequent episodes of associated hypoglycemia (Balzano & Piemonti, 2014). The extreme hypoglycemia is caused by peripheral insulin receptors being upregulated, with the insulin deficiency making them sensitive to insulin replacement, while hepatic insulin receptor availability is decreased. Because of pancreatic exocrine insufficiency and rapid intestinal transit, glucose malabsorption also increases the risk for hypoglycemia.

Islet autotransplantation (IAT) prevents PD or reduces the severity of PD. Pancreatic islet cell reimplantation has been performed since 1977 (Gala-Lopez, Semlacher, Manouchehri, Kin, & Shapiro, 2013; Iyegha, Asghar, & Beilman, 2012). Various sites have been used for implantation (e.g., splenic sinusoids, spleen, liver) (Brendle, 2010). The liver is the preferred site because of easy vascular access; the major complication of implanting islet cells in the liver is portal vein occlusion as a result of thrombosis.

IAT was initially developed for pancreaticectomy to treat chronic pancreatitis. However, a diagnosis of malignant disease is no longer an exclusion criterion for IAT (Iyegha et al., 2012). Previously, because of the theory of the multicentricity of multifocal intraductal papillary mucinous neoplasm, concern existed surrounding the infusion of carcinoma cells inside of the islet preparation. Multicentric pancreatic cancer is now not as common as previously assumed, and