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 pancreatogenic diabetes. 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 glycojenolysis 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 pancreatogenic 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 sinuses, 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 pancreatectomy 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...
incidence ranges from 0%–33% in the literature (Balzano & Piemonti, 2014). The theory of multicentricity of pancreatic cancer does not justify the additional morbidity and lifelong insulin dependence resulting from total pancreatectomy; no published evidence shows the occurrence of pancreatic malignant disease or metastases related to IAT in the liver (Iyegha et al., 2012).

Islet Cell Harvesting

After removing the pancreas, the surgeon cannulates the two pancreatic ducts and secures the canulas with suture. The surgeon then injects transplantation preservation fluid through the catheters to perfuse the pancreatic ductal system. The pancreas is then taken to a sterile laboratory with a biosafe hood. Any fat is removed, and a digestive enzymatic solution is infused into the pancreas through the canulas. The enzymatic solution consists of a blend of collagenase isofoms I and II and a thermostable neutral metalloproteinase enzyme. The infusion breaks down the pancreas, which is then dissected into 1 cm cubes. The pancreatic cubes are placed in a sterile bowl with plastic-coated marbles. Sterile tubing is attached to the two outlets on the lid. The tubing is placed in a pump filtration system that will collect the islet cells and the bowl into a shaker that allows the marbles to pulverize the pancreas cubes. The pancreas is broken down to the cellular level and pumped through the filtration system. The collected islet cells are placed in a centrifuge, where they are washed and centrifuged three times and then placed in a solution of 5% albumin. An average islet cell harvest yields 600,000–800,000 cells and is dependent on the condition of the pancreas (Brendle, 2010). A fibrous pancreas with extensive acinar damage yields fewer islet cells.

Islet Cell Transplantation

A catheter is placed in the portal vein of the liver and in the islet cells. The islet cells are infused and attach themselves to the liver vasculature. The liver then becomes an insulin-producing organ as the beta cells begin to produce insulin. The islet cells should start producing insulin within two to three days; however, the process may take longer.

Insulin drips and glucose monitoring occur during total pancreatectomy, beginning in the perioperative area (Balzano et al., 2013). Insulin drips are initiated in the operating room for glucose control. Optimum glucose goal is from 80–120 mg/dl (Chinnakotla et al., 2014). Intermittent insulin injections may be used with the insulin drip. Once basal insulin use is calculated, the patient is changed to basal insulin with sliding scale insulin coverage, and the insulin drip is stopped.

Hemodynamic stability, fluid and electrolyte balance, and adequate cardiopulmonary function are assessed during the immediate postoperative period (James, 2011). Nursing assessment of vital signs, intake and outputs, and assistance with pulmonary toilet is essential. IV fluid boluses or blood product transfusions with electrolyte replacement are necessary in the immediate postoperative period.

A heparin drip is infused at 10 units/kg for the first seven days postoperatively to prevent portal vein thrombus formation. The portal vein is evaluated by doppler ultrasound on day 1 and day 7 (Brendle, 2010). If the Doppler ultrasound detects any portal vein clots, anticoagulation with warfarin is continued for three months after surgery (Brendle, 2010).

Postoperative ileus is present in the immediate postoperative period because of anesthesia and bowel manipulation. A nasogastric tube is used for gastric decompression to prevent nausea and vomiting. An oral diet is started after the ileus resolves, which is indicated by decreased nasogastric tube output; discontinuation of the nasogastric tube is based on amount and color. The diet is advanced when the patient is able to take adequate calories and protein. Patients are educated about the use of pancreatic enzymes. The recommended initial dose of 1,000 lipase units/kg per meal, with a goal dose of 1,500 lipase units/kg per meal, is started (Chinnakotla et al., 2014). Pancreatic enzymes are increased based on patients’ symptoms, including diarrhea and weight loss, and the enzymes are titrated upward to eliminate those symptoms; the enzymes are adjusted during a period of several months. All patients are started on fat-soluble vitamin supplements (e.g., vitamin D, vitamin B_{12}). Patients are also instructed to avoid any heavy lifting for six to eight weeks postoperatively.

Postoperative Follow-Up

Patients are followed at 3, 6, and 12 months after surgery and then annually. Laboratory studies are obtained during these visits and include fasting glucose, c-peptide, and hemoglobin A1c to assess for metabolic control, islet graft function, and functioning beta cells. Height and weight are used to calculate patients’ body mass index, which is assessed for adequacy of pancreatic enzyme replacement.

Implications for Nursing and Conclusions

The nurse is an important member of the patient care team. Postoperative glucose management requires assessment of blood glucose and adjustment of insulin administration. As part of his or her role, the nurse must teach patients about the importance of checking their blood glucose, as well as factors that may affect glucose (e.g., illness). Patients, unless previously diabetic, will need to be taught how to use a glucometer and administer insulin. They also will need to be taught that pancreatic enzymes will need to be taken throughout their lifetime to prevent malabsorption of nutrients and malnutrition.

Total pancreatectomy with islet cell transplantation has been performed since the 1970s, initially for patients with chronic pancreatitis. However, the risk of seeding cancer cells into the liver by way of acinar and ductal tissue transplanted along with the islet cells has led to limited use of the procedure in oncology. Case reports have shown no recurrence of tumor in patients with malignancies receiving transplanted islet cells.

In addition, removal of the pancreas can lead to pancreatogenic diabetes, which is a difficult condition for patients and healthcare providers to manage and one that affects patients’ quality of life. Stabilizing patients with production of their own hormones through transplanted pancreatic islet cells improves glucose homeostasis. Further research is needed to document that autologous islet cell transplantation is a viable option for
patients undergoing total pancreatectomy for pancreatic cancer.

References


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