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Development of the Total Pancreatectomy and Autologous Islet Transplantation Models as the Step for Allogenic Islet Transplantation Experiments in the Swine

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Background: Islet transplantation has been established as a treatment for type 1 diabetes mellitus (DM). However, there are some problems to overcome, such as the necessity of transplantation from multiple donors repeatedly and the difficulty of achievement of the long term insulin independence. Creating an experimental model with large animal is extremely important as a preclinical study aiming to overcome those problems. We successfully established the total pancreatectomy combined with autologous islet transplantation model in the swine.
Materials and Methods: Thirteen swine weighing 10-20 kg underwent total pancreatectomy under general anesthesia. [Experiment 1] Eight swine underwent only total pancreatectomy (TP group), and the results of body weight, fasting blood glucose (FBS) and intravenous glucose tolerance test (IVGTT) before and after total pancreatectomy were compared and analyzed. [Experiment 2] Five swine underwent total pancreatectomy, then 50% of the excised pancreas were isolated by Ricordi method. Isolated pancreatic islets were autologously transplanted from portal vein into the liver (Islet Tx group) and their postoperative data was compared with that of TP group.
Results: [Experiment 1] Loss of body weight was significantly severer (+0.8 kg vs -1.9 kg, p=0.032) in 7 days after total pancreatectomy than in 7 days before total pancreatectomy. The value of FBS (49.4 mg/dl vs 327.0 mg/dl, p=0.001)) and IVGTT 120 min (84.0 mg/dl vs 364.7 mg/dl, p=0.044) were increased significantly after total pancreatectomy. Insulin secretion after glucose injection was not detected in this series. [Experiment 2] Compared with TP group, the loss of body weight was mild (-1.9 kg vs -0.1 kg, p=0.22), and the survival rate was significantly increased (38% vs 100%, p=0.035) in Islet Tx group. The value of postoperative FBS (327.0 mg/dl vs 97.4 mg/dl, p=0.001) and IVGTT 120 min (364.7 mg/dl vs 153.5 mg/dl, p=0.016) were significantly lower in the Islet Tx group. In the Islet Tx group, insulin secretion after glucose injection was detected. This is because transplanted islets were survive and functioning. Pathological specimens on the 7th day after islet transplantation showed the engraftment of transplanted pancreatic islets into the intrahepatic portal vein.
Conclusions: We successfully established the insulin dependent DM model by using total pancreatectomy in the swine. We also successfully established the total pancreatectomy and islet autotransplantation model in the swine. Improvement in the outcomes of islet transplantation would be expected by developing this model to allogeneic islet transplantation experiments.

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Early Infectious Complications Post Total Pancreatectomy with Islet Autotransplantation

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Introduction: Infectious complications (IC) after pancreatic surgery occur in about 30% of patients. Although IC have not been extensively studied in patients submitted to total pancreatectomy with islet autotransplantation (TPIAT), it has been shown that microbiological contamination of the final islet preparation has no effect on the risk of developing infection. The aim of the study was to evaluate the prevalence, etiology and outcomes of all IC early after TPIAT with reference to the preservation fluid and islet preparation cultures.
Methods: We performed a retrospective cohort study reviewing medical records of patients submitted to TPIAT at the University of Chicago Medicine between January 2014 and October 2017. We analyzed preservation fluid and islet cultures with reference to clinical data. All patients received broad-spectrum antibiotic prophylaxis during the surgery.
Results: We studied data from 23 patients after TPIAT due to chronic pancreatitis and intractable pain (14 women and 9 men), with a mean age of 36 ± 14years. Most common IC were wound infections (22%), followed by PICC line associated bacteremia/fungemia (13%) and catheter associated urinary tract infections (9%). Seven preservation fluids (30%) and 8 islet preparations (35%) showed positive microbial growth with a majority due to Gram-positive or Gram-negative intestinal flora and common polymicrobial contaminations (10 of 15 [66.6%]). Five patients (22%) had both positive preservation fluid and islet cell culture from the final islet preparation solution. Of those, 3 individuals developed complications- 1) fever without a clear source that required intravenous antibiotics, 2) pneumonia and 3) sepsis, wound infection and dehiscence, together with small and large bowel perforation. Two patients had positive preservation fluid cultures alone and only one of them developed a wound infection. Two out of 3 patients with positive islets cultures alone had IC, one developed a fever of unknown source and later a wound infection, while another one catheter associated urinary tract infection. None of the infections concurred with the positive preservation fluid or islet product cultures. In 17 patients with both sterile preservation fluid and final islet product, three had a PICC line related bacteremia/fungemia and two developed wound infections. Four out of 5 patients with early wound infections developed hernias in the late postoperative course. There were also 3 cases of hernia without prior wound infection.
Conclusions: Infectious complications are a common problem in patients undergoing TPIAT and wound infections represent a consistent proportion and a risk factor for subsequent hernia development. Positive islet cultures may result from colonization and may be a marker of increased susceptibility to symptomatic infections, while positive preservation fluid culture alone seems to result from contamination during surgery and does not affect the outcome.