Abstract (English)

Perfluorocarbons (PFC) are hydrocarbons in which some or all of the hydrogen atoms are replaced with fluorine. PFC have a very high capacity for dissolving oxygen. They are chemically and biologically inert. The most successful clinical application of PFC is the "two-layer method" for pancreas preservation before islet isolation. The two-layer organ preservation method (TLM) is based on oxygenated perfluorocarbon overlaid with University of Wisconsin (UW) solution. In experiment it has been successfully used for heart and intestine transplantation. We tested whether this technique would prevent tissue damage and improve results of kidney, pancreas and islets of Langerhans transplantation with prolonged ischemia time in an experimental model of syngenic rats. In kidney and islets of Langerhanse transplantation model we used TLM preservation method. In pancreas transplantation model we used perfluorohexyloctane (PFH) as a new generation of less lipophilic PFC.

1. Kidneys were stored for 24 hours either in UW solution (n = 16), with TLM (n = 16) or transplanted immediately (control group, n = 12). In half of the animals, survival was observed and in the other animals grafts were procured for semiquantitative histological scoring and TUNEL apoptosis assessment 24 h after transplantation. One-month survival rates in the UW, TLM and control groups were 12.5, 62.5 and 100%, respectively (UW vs. TLM, p<0.01). Median creatinine levels 24 h after transplantation were 381, 299 and 121 µmol/l, respectively (UW vs. TLM, p<0.02). Histological scoring showed more severe tissue damage in the UW group than in the TLM group (p<0.05). Apoptosis was more frequent in the UW group than in the TLM group (p<0.05). In this experiment we demonstrated that conservation with PFC as a component of the "two-layer method" significantly improves the outcome of kidney transplantation in a rat model.

2. In the next step, we tested impact of TLM on islet isolation and transplantation. Pancreata were stored for 24 hours in UW solution (n=39), with TLM (n=35) or used for islet isolation immediately without preservation (n=10). We proofed significantly higher islet yield and improved outcome after transplantation using TLM compared to conventional static cold preservation in UW solution.

3. In the model of pancreas transplantation we evaluated the impact of perfluorohexyloctane on long-term cold storage in a rat whole pancreas transplantation model. Brown-Norway rats were used for syngeneic heterotopic pancreas transplantation. The procured organs were cold-stored for 18 hours in preoxygenated PFH (PFH group) (n=8) or in the University of Wisconsin solution (UW group) (n=8) or were transplanted immediately in the control group (n=8). Two hours after reperfusion, we obtained blood and pancreas tissue samples for biochemistry and gene analyses (real-time PCR). A significant difference between the UW and PFH group was observed in the TNFβ and endothelin 1 genes, which was overexpressed more than twofold in the UW group. In the blood samples, the UW group compared with the PFH group showed significantly higher levels of pancreatic amylase and lipase (94.2±25.2 vs. 67.7±13.4 µkat/l and 5.5±2.8 vs. 3±0.7 µkat/l, respectively; p< 0.05). These findings suggest lower rate of ischaemic reperfusion injury in the PFH group.

In our experiments we confirmed superiority of long-term cold storage with PFC for kidney, pancreas and islets of Langerhans transplantation compared to conventional cold preservation in UW solution.