Use of UW Solution in Pancreas Transplantation

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We have recently reported successful 72-h preservation of the canine pancreas with a new cold-storage solution developed at the University of Wisconsin (UW solution). Over 10 mo, we performed 11 combined pancreas-kidney and 4 isolated-pancreas transplants with this solution. In situ cooling of the donor pancreas was performed with 1000 ml of UW solution followed by ex vivo perfusion with an additional 250–500 ml. Graft preservation times ranged from 3 to 19 h (mean 10.2 h). Pancreas transplants were vascularized whole-organ grafts with pancreaticoduodenocystostomy. Early graft function was excellent as assessed by immediate insulin independence, high urinary amylase and low serum amylase levels, and a technetium perfusion index indicating good pancreatic blood flow. There were no episodes of primary nonfunction, graft pancreatitis, or vascular thrombosis. Actuarial patient and graft survival at 1 mo was 92.9%. We conclude that UW solution provides excellent early graft function for up to 19 h of cold storage. Based on previously reported data on its efficacy in liver and kidney preservation, UW solution seems ideally suited as a universal intra-aortic flush and cold-storage solution. *Diabetes* 38 (Suppl. 1):7–9, 1989

Successful 72-h preservation of the canine pancreas has been obtained with a solution that has as its major components K^+-lactobionate, raffinose, and hydroxyethyl starch (1). This solution has also been used both experimentally and clinically in liver and kidney transplantation with encouraging results (2–4). The advantages of longer preservation times are obvious and include less urgent operations, the availability of more organs, and prospective cross matching and tissue typing.

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Between May 1987 and February 1988, we used UW solution as an intra-aortic flush and cold-storage solution in 15 cadaveric pancreas allografts. In this article, we report our results with this solution in clinical pancreas transplantation.

MATERIALS AND METHODS

Over a 10-mo period, 15 whole-organ vascularized pancreas transplants were performed after cold-storage preservation with UW solution [(in mM) 100 K^+-lactobionate, 25 KH_2PO_4, 5 $MgSO_4$, 30 raffinose, 5 adenosine, 3 glutathione, 1 allopurinol, 30 ± 5 Na^+, 120 ± 5 K^+; 100 U/L insulin; 0.5 ml/L Bactrim; 8 mg/L dexamethasone; and 50 g/L hydroxyethyl starch; pH 7.45, osmolarity 320 ± 5 mosM]. Preservation times ranged from 3 to 19 h, with a mean preservation time of 10.2 h. The mean recipient age was 34.6 yr (range 22–48 yr), with a mean duration of type I (insulin-dependent) diabetes of 22.2 yr (range 15–37 yr). Eleven patients received combined pancreas-kidney transplants, whereas 4 underwent isolated pancreas transplantation. All 4 patients receiving an isolated-pancreas transplant had undergone a previous kidney transplant: 3 from living related donors and 1 from a living unrelated donor.

Pancreas procurements were from braindead donors, 13 of which required dopamine (mean dose 8.4 ± 5.6 $\mu g \cdot kg^{-1} \cdot min^{-1}$) at the time of retrieval. After pancreatic dissection, the donor was given 10,000 U i.v. heparin and 10 mg i.v. Regitine. In situ aortic flushout with 1000 ml UW solution followed by ex vivo perfusion with an additional 250–500 ml was used. The graft was placed in a sterile plastic bag containing 500 ml UW solution, kept on ice, and stored at 4°C until transplantation.

Pancreas transplantation was then performed as previously described (5). Briefly, the pancreas was vascularized by an end-to-side anastomosis of the portal vein to the external iliac vein followed by an end-to-side anastomosis of a Carrel patch containing both the celiac and superior mesenteric arteries to the external iliac artery. Pancreaticoduodenocystostomy with a duodenal segment (6) was used to divert exocrine secretion into the urinary bladder. Patients receiving a combined pancreas-kidney transplant under-

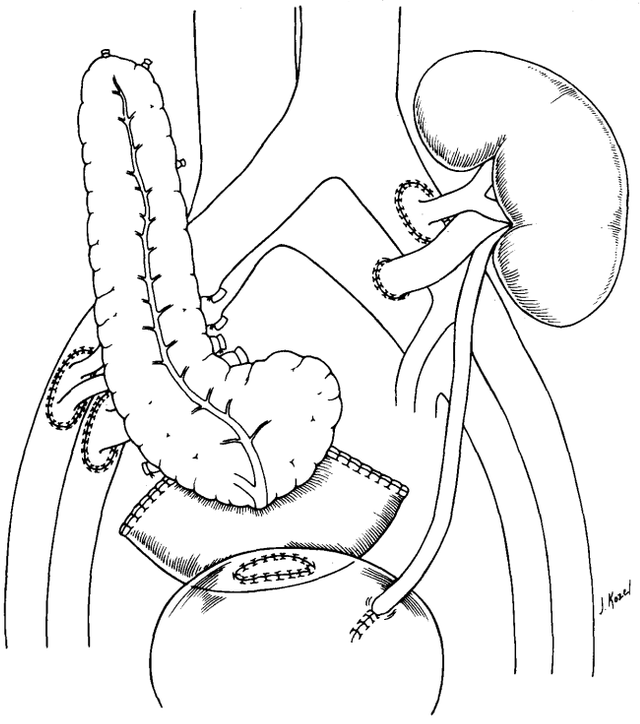

FIG. 1. Technique of combined pancreas-kidney transplantation with pancreaticoduodenocystostomy for exocrine drainage.

went an intra-abdominal kidney transplant in the opposite iliac fossa with standard techniques after the pancreas implantation was completed (Fig. 1).

Parameters of early graft function included urinary amylase (UA; normal >10,000 U/L), serum amylase (SA; normal 20–100 U/L), fasting blood glucose (FBG; normal 70–110 mg/dl), and a technetium perfusion index (TI; normal >0.3). TI (^{99m}Tc-labeled DTPA) is a quantitative measure of blood pooling in the pancreas allograft determined by computer analysis of the percentage of tracer present in the graft after the 2nd min of scanning (7). Overall graft function was evaluated, including the effect of preservation time on allograft function. Patients were divided into three groups according to the length of preservation: group 1, <6 h (n = 4); group 2, 6–12 h (n = 6); and group 3, >12 h (n = 5). Quadruple immunosuppression consisting of prednisone, azathioprine, and the sequential use of Minnesota antilymphoblast globulin (ALG), and cyclosporin was used. Rejection episodes were treated with pulsed steroids, ALG, or OKT3.

Statistical Analysis. Data are reported as means ± SD. Differences between groups were compared with Student's t test. $P < .05$ was considered significant.

RESULTS

All pancreas allografts functioned immediately, with complete insulin independence achieved after implantation. There were no cases of primary nonfunction, graft pancreatitis, or vascular thrombosis. Mild elevations in SA were noted but were not clinically significant. UA levels rose steadily and attained normal levels by day 3. FBG was slightly elevated in the immediate postoperative period but normalized within 1 wk. Radionuclide scanning with technetium revealed excellent perfusion on the 1st postoperative day, with a mean TI of 0.45 ± 0.19 (Table 1).

No significant difference in graft function was detected between the three groups at 24 h. However, a significantly lower UA level was seen at the time of discharge in grafts preserved for >12 h (Table 2). Actuarial patient and graft survival at 1 mo was 92.9%. One patient died with a functioning graft from cerebral anoxia after a postoperative respiratory arrest. Seven patients (46.7%) experienced a rejection episode within the 1st mo posttransplantation; four were reversed with OKT3, one with goat ALG, and two with pulsed corticosteroids.

DISCUSSION

Until recently, preservation of the pancreas beyond 6 h was not recommended, primarily because of graft pancreatitis and vascular thrombosis reported with Collins solution (6,8,9). Longer preservation times have been reported by Abouna et al. (10) and Florack et al. (11) with silica gel–filtered plasma and, more recently, modified plasma protein fraction (12,13). Wahlberg et al. (1), from our institution, reported successful 72-h canine pancreas preservation with UW solution. Our results demonstrate successful human pancreas-allograft preservation for up to 19 h of cold storage without graft pancreatitis, primary nonfunction, or vascular thrombosis. The reason for the lower UA levels at the time of discharge in grafts preserved for >12 h is not known but may represent a minor loss of pancreatic exocrine function. Our experience with pancreas transplantation before the use of UW solution demonstrated a significantly lower early postoperative UA level (data not included). UA levels, which we and others (14–16) use to monitor allograft rejection, also appear to be a sensitive indicator of the quality of preservation. The TI indicates good early pancreas-allograft perfusion but appears to have as its major advantage the monitoring of transplant rejection (7). SA, with the exception of early severe graft pancreatitis, which we did not observe, may not be a good indicator of preservation as suggested by Abouna et al. (10). This may, however, represent the improved overall quality of pancreas preservation for extended periods with these newly developed solutions. Over-

TABLE 1
Overall graft function

	Urinary amylase (U/L)	Fasting blood glucose (mg/dl)	Serum amylase (U/L)	Tc index (%)
Day 1	8329 ± 7924	115.6 ± 43.6	216.3 ± 149.1	0.45 ± 0.19
Day 3	14,394 ± 13,382	130.3 ± 23.7	154.0 ± 158.4	
Discharge*	31,770 ± 17,712	84.8 ± 5.9	156.3 ± 89.6	

*Length of hospitalization 21.4 ± 5.6 days.

TABLE 2
Effect of preservation time on graft function

	Graft function at 24 h*	Graft function at discharge
Fasting blood glucose (mg/dl)		
Group 1	142 ± 51.0	88.3 ± 5.1
Group 2	107.3 ± 37.1	81.2 ± 6.1
Group 3	104.4 ± 45.0	86.8 ± 4.6
Urine amylase (U/L)		
Group 1	3,125 ± 3,079	45,056 ± 16,612
Group 2	11,548 ± 10,531	36,689 ± 12,423
Group 3	9,785 ± 8,966	15,020 ± 11,847†
Serum amylase (U/L)		
Group 1	254.3 ± 145.8	170.0 ± 79.4
Group 2	287.3 ± 169.6	192.6 ± 114.2
Group 3	120.6 ± 40.8	100.3 ± 35.5
Technetium perfusion index (%)		
Group 1	0.41 ± 0.22	
Group 2	0.55 ± 0.16	
Group 3	0.41 ± 0.18	

Values are means ± SD. Preservation time: group 1, <6 h (n = 4); group 2, 6–12 h (n = 6); group 3, >12 h (n = 5).
*NS between groups at any parameter.
†$P < .05$.

all, the high UA, low SA, complete insulin independence, and good pancreatic perfusion indicate preservation of both exocrine and endocrine function of the pancreas. Based on these findings, we recommend UW solution for cold-storage pancreas preservation. The encouraging results in liver and kidney preservation with this solution reported previously indicate that it may be ideally suited as a universal cold-storage solution.

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