Clinical Pancreas Transplantation

Influence of Serum Amylase and Plasma Glucose Levels in Pancreas Cadaver Donors on Graft Function in Recipients

UWE J. HESSE AND DAVID E.R. SUTHERLAND

In a series of 101 pancreas transplants from brain cadaver donors, serum amylase levels were determined preoperatively in 47 donors, and plasma glucose levels were monitored in 94 donors. Eighty-six percent of the donors died from head injury and 14% from asphyxia. No donors had a history of diabetes or pancreatitis, and the pancreas was grossly normal in all donors. Of the 47 cadaver pancreas donors in whom serum amylase levels were measured, the values of 20 donors were elevated (110–994 IU/L), and the values of 11 donors were >300 IU/L. In 51 of 94 braindead cadaver pancreas donors in whom plasma glucose determinations were made, hyperglycemia was present (200–980 mg/dl). Early posttransplant pancreas-graft function was excellent in all recipients except for 5 patients in whom the grafts had to be removed for reasons not related to donor serum amylase and plasma glucose levels. Hyperamylasemia and hyperglycemia are probably not contraindications for cadaver pancreas organ donation unless overt pancreatic trauma, pancreatitis, or a history of diabetes is present. *Diabetes* 38 (Suppl. 1):1–3, 1989

Criteria for pancreas donation regarding the functional status of the donor and the donor organ have been well defined for grafts from living related donors (1,2), but there is little information about this issue for cadaver donors. Direct abdominal trauma involving the pancreas and a history of diabetes and pancreatitis in a potential donor are contraindications for organ procurement and transplantation (3). However, serum amylase and plasma glucose levels are often abnormal in polytraumatized (4) and cranially traumatized (5,6) individuals. The status of the cadaver pancreas in regard to exocrine and endocrine function is difficult to assess in a potential cadaver organ donor with these conditions. In this study, the influence of cadaver donor serum glucose and amylase levels on the functional status of the pancreas after successful transplantation into diabetic recipients was evaluated.

From the Department of Surgery, University of Minnesota Hospital, Minneapolis, Minnesota.

Address correspondence and reprint requests to Dr. David Sutherland, Box 280, University of Minnesota Hospital, 420 Delaware Street, SE, Minneapolis, MN 55455.

MATERIALS AND METHODS

The profiles of 101 cadaver pancreas donors used in the University of Minnesota pancreas-transplant program between 25 July 1978 and 25 July 1986 were retrospectively reviewed for cause of death, serum amylase, plasma glucose, graft-preservation time, and warm-ischemia time. The donors were all braindead with beating hearts and were receiving artificial respiration.

Solu-Medrol (500–3000 mg) and Decadron (4–36 mg) were given to all donors during the period of respiratory support. Renal insufficiency was absent in all donors, and the kidneys were suitable for transplantation. Just before and during organ procurement, insulin was administered on a sliding scale, based on plasma glucose levels with objectives to maintain levels around or under 100 mg/dl. In 33 instances, the pancreas graft was transplanted immediately after removal from the donor, whereas in 68 cases the grafts were preserved from 1 to 26 h (mean ± SE 10.9 ± 5.5 h) in either Collins solution (1 case) or silica gel–filtered plasma at 4°C as previously described (7,8). Fifty-six pancreases were transplanted as whole organs and 45 as segmental grafts with the body and tail. Exocrine drainage was performed as open-duct intraperitoneal drainage in 10 patients, duct ligation in 3, duct injection in 35, pancreaticojejunostomy in 36, and pancreaticocystostomy in 17. Ninety-six grafts were anastomosed to the iliac vessels and situated intraperitoneally, whereas for 5 grafts, vascular anastomoses were to the inferior mesenteric artery and vein. The patients were immunosuppressed with azathioprine and prednisone, cyclosporin and prednisone, or triple therapy consisting of azathioprine, cyclosporin, and prednisone. The details of surgical technique and patient management have been de-

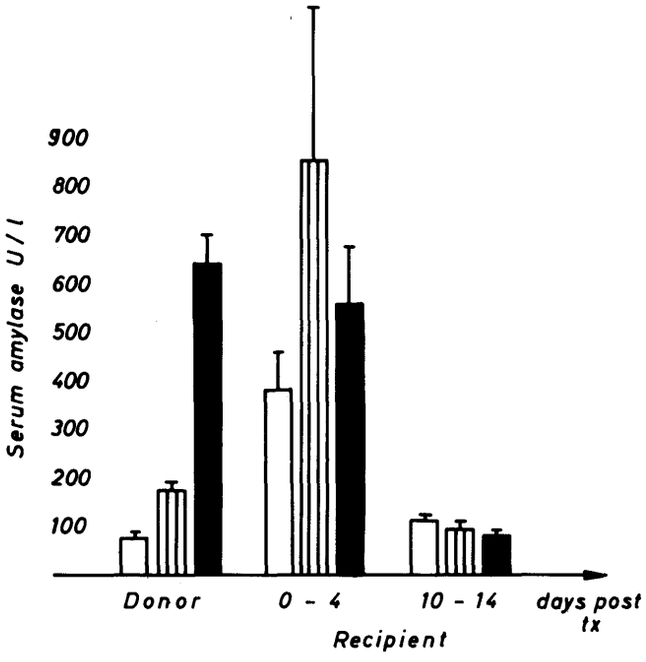

FIG. 1. Serum amylase (U/L; means ± SE) in donors (*solid bars*, >300 U/L; *lined bars*, 110–300 U/L; *open bars*, <110 U/L) and in corresponding recipients at days 1–4 and 10–14 posttransplant.

scribed (9–11). Serum amylase, plasma glucose, and other parameters were measured daily in the clinical laboratory and were used to determine transplant function.

A plasma glucose level between 80 and 120 mg/dl was considered normal when the patient was off insulin. Serum amylase levels <110 IU/L were considered normal. Serum amylase levels in 47 recipients during days 1–4 and 10–14 posttransplant were compared with the values in the corresponding 47 cadaver donors, and plasma glucose levels measured in 94 transplanted patients were compared with the levels in the corresponding 94 cadaver donors. Before transplantation, all recipients had normal amylase values but were insulin dependent.

Eighty-seven donors (86%) died from head injuries, 58 from motor-vehicle accidents, 16 from cerebral vascular accidents, 6 from gunshot wounds, 2 from sport activities, and 5 from fall injuries. Fourteen donors (14%) died from asphyxia (3 from asthma, 2 from smoke intoxication, 3 from suicide by hanging, 2 from drowning, and 4 from undefined causes).

RESULTS

Serum amylase levels in the 47 cadaver donors in which it was measured ranged from 12 to 994 IU/L (mean ± SE 212 ± 26.5 IU/L, normal range 50–110). Serum amylase levels were within the normal range in 27 donors (55 ± 4 IU/L) and were elevated in 9 donors (174 ± 15 IU/L). Eleven donors had extreme elevations of serum amylase (638 ± 68 IU/L). The corresponding serum amylase levels in the recipients during the first 4 days and 10–14 days posttransplant were 383 ± 85 and 108 ± 14 IU/L, 853 ± 314 and 95 ± 17 IU/L, and 550 ± 228 and 82 ± 10 IU/L, respectively (Fig. 1). There was no apparent correlation between the donor serum amylase and the recipient posttransplant serum amylase levels, and none of the pancreases procured from donors with highly elevated serum amylase levels showed any gross signs of pancreatitis at the time of organ removal. The serum amylase levels in all recipients were normal by ≥2 wk posttransplant.

Early in the posttransplant period, none of the recipients of grafts from donors with highly elevated serum amylase levels (n = 11) developed a clinical pancreatitis picture or any other pancreatic complication that can be related to the exocrine pancreas, except for one patient whose functioning graft had to be removed for pancreatitis 2 wk posttransplant, presumably because of a herpes infection that was demonstrated in the graft. However, serum amylase at the time was decreased from 1262 to 93 IU/L, whereas the serum amylase in the donor was 384 IU/L. In a second patient a functioning graft had to be removed for pancreatitis 1 mo posttransplant. However, the amylase in the donor was 50 IU/L, and plasma glucose was 324 mg/dl.

Plasma glucose levels were measured in 94 donors and showed values between 49 and 980 mg/dl (median 227, mean ± SD 295 ± 178 mg/dl). Plasma glucose levels were >400 mg/dl in 11 donors, 200–400 mg/dl in 40 donors, and <200 mg/dl in 43 donors. Endocrine function as assessed by plasma glucose levels after cessation of insulin was good in all but five of the recipients. There was no apparent correlation between plasma glucose levels in the donors and the early plasma glucose levels in the recipients.

A total of five grafts never functioned or had to be removed within the first 2 days posttransplant, but the poor function has to be attributed to factors unrelated to the plasma glucose or serum amylase levels (Table 1). One patient received a graft that had been removed from a heart donor in which there was a 30-min period of warm ischemia between cessation of heartbeat and removal of the pancreas, which was followed by a preservation time of 11 h. The plasma glucose level in this donor was 253 mg/dl. The other patient received a graft that was preserved for 26 h, the longest preservation time in this series. The donor plasma glucose level was 231 mg/dl. In both cases, it was felt that the lack of function was related to prolonged preservation time or prolonged warm-

TABLE 1
Grafts that primarily failed or had to be removed within first days posttransplant

Technique	Donor amylase (IU/L)	Donor glucose (mg/dl)	Warm-ischemia time (min)	Cold-ischemia time (h)	Cause of failure
Duct injected		253	30	11	Preservation failure
Enteric drained		231		26	Preservation failure
Enteric drained	116	257		11	Bleeding from graft
Bladder drained		264		10	Venous graft thrombosis
Bladder drained	165	65		19	Venous graft thrombosis

ischemia time. Two more patients' grafts failed because of venous thrombosis of the graft, and the fifth patient's functioning graft had to be removed for bleeding 12 h posttransplant.

There was no statistically significant difference in long-term (1-yr) graft survival between recipients of grafts from donors with normal, elevated, and extremely elevated serum amylase or plasma glucose levels as calculated by the Mantel-Cox test.

DISCUSSION

Elevated serum amylase and plasma glucose levels in a cadaver donor are usually unrelated to the functional status of the pancreas graft. Neither parameter appears suitable to use for exclusion criteria in the evaluation of pancreatic function. Ninety-five percent of the pancreas grafts in this analysis functioned in the early posttransplant period despite the fact that 51 of 94 (54%) grafts were procured from hyperglycemic donors (i.e., blood glucose >200 mg/dl). Of the 47 donors in whom amylase was measured, the levels were above normal in 20 (43%). Five grafts (5%) in the entire series did not function, but the failure appeared not to be related to pancreatitis or any other pancreatic disorder in the donor. Only two grafts had to be removed for pancreatitis 14 days and 1 mo posttransplant, and the corresponding donors did not have evidence of pancreatitis. Pancreatitis was diagnosed clinically in this series and was not based on graft biopsies as proposed by Squifflet et al. (12).

The rise in posttransplant amylase values in our recipients was similar to that reported by the Stockholm group (13), which was attributed to the addition of an extra pancreas. Another explanation for raised amylase levels in transplant recipients relates to steroid administration, which has been shown to increase the serum concentration of all pancreatic enzymes (14).

Because graft function was comparable in the recipients regardless of whether the grafts were procured from donors with normal, elevated, or highly elevated glucose or amylase levels, the hyperglycemia in cadaver donors is attributed to the liberal administration of intravenous glucose solutions and the administration of exogenous steroids. In addition, the release of hormones such as steroids and catecholamines in response to stress might also be responsible for the elevated plasma glucose levels. Hyperamylasemia in potential cadaver donors could be caused by direct involvement of the pancreas with trauma, a situation that should exclude the cadaver as a donor. However, in our cases, hyperamylasemia was seen without any evidence of direct trauma to the pancreas. Eighty-six percent of our donors died of cranial trauma, and 14% were brain dead due to various other reasons. Head injury and other trauma not involving the pancreas is often associated with hyperamylasemia (4–6). Other causes of hyperamylasemia are metastatic cancer and renal insufficiency (15), but such diseases were absent in all our donors and thus could not be responsible for the hyperamylasemia.

The analysis summarized here includes only the pancreas transplants performed up to 1986. Most transplants in this early cohort were performed by the duct-injection and enteric-drainage techniques, and none were simultaneous with a kidney. With these approaches, only plasma glucose can be used to monitor graft function. Elevation of plasma glucose is a late manifestation of rejection and is usually irreversible. Because the early rejection rate is high, an adverse effect with use of grafts from hyperglycemic donors on long-term graft function might have been masked in the cohort we studied. Since 1986, most of our pancreas transplants have been performed by the bladder-drainage technique (16). With this technique, urinary amylase activity can be monitored as a direct measure of graft function; rejection is manifested by a decrease in urinary amylase activity before an elevation of plasma glucose occurs, and most rejection episodes can be reversed by early treatment (11). Thus, the current graft functional survival rates, with bladder drainage exclusively, are significantly higher than in the earlier cohort (16). The influence of donor plasma glucose and serum amylase levels on long-term survival rates of bladder-drained grafts remains to be determined and is the subject of a prospective study. However, we do not exclude donors on the basis of hyperamylasemia or hyperglycemia as long as there is no history of diabetes and no apparent abnormality of the pancreas at the time of organ retrieval.

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