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# Simultaneous Pancreas and Kidney Transplantation: First Report from Shahid Beheshti University of Medical Sciences and Review of Anesthesia Considerations

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## ABSTRACT

We report a 33 year-old woman presented with signs and symptoms of severe uncontrolled diabetes mellitus and chronic renal failure (diabetic nephropathy). She was prepared for emergency simultaneous pancreas and kidney transplantation (SPK) using hemodialysis and after compensating for the acid – base abnormality. She was discharged from the hospital about 3 week after the surgery with good renal and pancreatic function. A 2-month follow-up revealed no complication and a good renal and pancreatic function. Due to the importance of this kind of treatment and several anesthetic considerations of SPK we present this case report along with some pearls about related anesthetic view points. (*Tanaffos*2010; 9(4): 69-74)

**Key words:** Simultaneous Pancreas and Kidney Transplantation, Anesthesia, Transplantation

## INTRODUCTION

At the turn of the 20<sup>th</sup> century, before the isolation of insulin, grafting of portions of pancreas to treat diabetes was actually attempted (1,2). In 1929, Banting proposed transplantation of the insulin-producing tissue of the pancreases (3). Lillehei and colleagues performed the first pancreas transplant to treat diabetes in humans in 1966 at the University of Minnesota, as reported by Kelly et al (4). They did a combined pancreas and kidney transplant in two

patients with long-standing diabetes and far-advanced secondary complications. One patient died of complications related to surgery. The other had satisfactory graft function and remained normoglycemic and insulin independent for nearly 6 months post transplant. The success rate for pancreas transplantation was initially very low, but it has constantly improved due to better surgical techniques and introduction of cyclosporines. Approximately 1000 cadaver transplants are now done yearly in 150 centers internationally. One-year graft and patient survival rates are now 70% and 91%, respectively (5,6,7,8). Currently, the most common surgical options are simultaneous pancreas and kidney

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transplantation (SPK) for uremic patients, pancreas after kidney transplant (PAK) for chronically immunosuppressed recipients, and pancreas transplantation alone (PTA) for nonuremic and no kidney recipients. SPK is the most common pancreas transplantation performed worldwide. Of the 5,807 transplants performed between January 1968 and April 1994 reported to international pancreas transplant registry, 80% were SPK. Adding pancreas graft to a kidney graft is justified for three reasons:

1. Patients are already obligated to immunosuppression therapy due to the kidney transplant, and it is generally accepted that quality of life is better when immunosuppressed and dialysis free than non-immunosuppressed and dialysis dependent (9).
2. It may prevent recurrence of diabetic nephropathy in the allograft (10).
3. Quality of life improves even if insulin independence is the only benefit achieved other than reversal of uremia, with only minimal additional surgical risk.

If diabetic patients hope to achieve and maintain normal blood glucose levels, therapeutic alternatives to standard insulin treatment must be sought. Pancreas transplantation is the only current method that consistently normalizes serum glucose levels (5). Despite some valuable progresses in fields of transplant organ procurement and different kinds of organ transplantation in Iran at recent years, unfortunately; we have limited experiences about simultaneous pancreas and kidney transplantation. This is due to difficulties of patient selection and preparation and also technical difficulties in both fields of anesthesia and surgery as well as proper post operative intensive care. We have valuable experiences about lungs, heart, kidney and some other kinds of organ transplantation in our centers but nothing about SPK. Many patients with simultaneous kidney (chronic renal failure) and pancreas disease (insulin dependent diabetes mellitus ) exist that suffer

from these conditions and need aggressive therapy such as SPK for curative treatment. This is the report of the first, successful SPK transplantation conducted at a medical center affiliated to Shahid Beheshti University of Medical Sciences. Due to the importance of this kind of treatment and several anesthetic considerations of SPK we present this case report along with some pearls about related anesthetic view points(11).

## CASE SUMMARIES

A 33-year-old woman presented with signs and symptoms of severe uncontrolled diabetes mellitus. The disease was diagnosed about 5 years ago but it seemed that the condition had existed for a long time before the diagnosis. She also had signs and symptoms of chronic renal failure (diabetic nephropathy) since last year with severe rising in creatinine and blood urea nitrogen. The patient was under hemodialysis for the last 6 months. She also had signs of diabetic retinopathy with bilateral retinal detachment and visual loss which were treated by deep vitrectomy of both eyes. After bilateral vitrectomy she developed visual acuity for light perception. At the time of admission, she had high levels of fasting blood sugar (about 271 mg/dl), raised levels of BUN and creatinine and mild degrees of metabolic acidosis. She was prepared for emergency simultaneous pancreas and kidney transplantation (SPK) using hemodialysis and after compensating for the acid – base abnormality. Kidney and pancreas procurement was done at Masih Daneshvari Hospital, the referral center for transplant organ procurement, from a brain dead patient and the organs were immediately sent to Labbafinejad Hospital where the transplantation team was well prepared for the surgical operation. The patient was transferred to the operating room and anesthesia was induced with intravenous administration of propofol, alfentanil and atracurium. Tracheal intubation was done using a low pressure No. 7.5 tracheal tube and

maintained with TIVA method using remifentanyl, atracurium and propofol. The operation took a long time (about 9 hours) during which sequential kidney and pancreas transplantation was done without any serious complications.

There was no serious anesthesia related complications during the procedure, except for two important events during this time; first, a transient metabolic acidosis at the time of pancreatic duct implantation and second, a hyperglycemic attack (289 mg/dl) soon after the beginning of pancreas transplantation. Both of these events were managed properly. The effect of neuromuscular blocking agent was reversed at the end of surgery and the patient was extubated early at the end of the procedure after insuring her optimal homodynamic, metabolic and general conditions.

She was transported to the intensive care unit for precise control and monitoring. The patient became oliguric at day 3 after transplantation which resolved gradually by day 5 after surgery using appropriate management. The patient became normoglycemic by day 2 post operation. She was discharged from the hospital about 3 week after the surgery with good renal and pancreatic function. A 2-month follow-up revealed no complication and a good renal and pancreatic function.

### ***Anesthesia Considerations:***

#### ***Pretransplantation evaluation (11):***

Before the anesthesiologist visit, patients scheduled for a pancreas or combined pancreas and kidney transplantation undergo a thorough assessment by an endocrinologist and the transplant surgeon to confirm the diagnosis of type 1 diabetes. All patients are evaluated for presence of other secondary diabetic complications including retinopathy, nephropathy, and neuropathy.

#### ***Preoperative evaluation (11,12,13)***

Except in the rare case of living-related segmental pancreas donation, pancreas transplantation is

performed soon after a cadaver organ is available. Because the preservation time is usually limited to less than 24 hours (14), anesthesiologists must work under emergent or semi urgent conditions. In spite of time constraints, a thorough presurgical evaluation is essential before administering the anesthetic drug. Most patients undergoing pancreas, islet cell, or combined kidney-pancreas or islet cell transplantation have severe systemic complications of longstanding diabetes mellitus, including coronary artery disease, severe hypertension, renal insufficiency, autonomic and systemic neuropathy as well as gastroparesis. Special consideration should be given to evaluation of the airways in patients undergoing pancreas transplantation (15). The cause of increased difficulty with intubation in diabetic patients is not known (16). The immediate pretransplantation status of cardiac and pulmonary systems must be studied. Cardiac disease can affect both homodynamic stability and long-term patient and allograft survival. Neuropathy, both systemic and autonomic, is common in pancreas transplant recipients.

Electrocardiograms should also be examined for resting tachycardia, which may indicate vagus nerve dysfunction. Neuropathy of the vagus nerve induces gastroparesis, which increases the risk of aspiration of gastric contents (17,18).

Motor and sensory peripheral neuropathy is common (15,19). Severe motor neuropathy caused by diabetes or uremia may increase the risk for hyperkalemia after succinylcholine administration (20). Evaluation of the preoperative metabolic status is essential because many pancreas transplantation patients have extremely brittle diabetes or renal insufficiency. It is important to obtain preoperative electrolytes and serum creatinine levels as well as the timing of last dialysis in dialysis-dependent patients. Hyperkalemia (potassium greater than 5.5 mol/liter) should be treated preoperatively either with insulin (if associated with hyperglycemia) or with ion exchange resins.

**Induction (11):**

A pancreas transplant, particularly if combined with a renal transplant, can be a long (8-9 hours) procedure. For this reason, general anesthesia is always used. Anesthesia is usually induced intravenously with a small dose of narcotic (fentanyl or alfentanil) and either a barbiturate (thiopental) or etomidate. Etomidate is preferred over thiopental in case of significant cardiac disease or autonomic neuropathy because it causes minimal cardiac depression and maintains the automatic tone. Adrenal suppression has been reported after etomidate administration (21); however, transplant recipients receive relatively high dose of corticosteroids for immunosuppression. After administration of the hypnotic agent, a skeletal muscle relaxant that does not depend on renal excretion (e.g., vecuronium or atracurium) is administered. The patient is orotracheally intubated. Slick's maneuver should always be applied before intubations because patients may have gastroparesis that they are not aware of. If the patient has not been NPO (for 8 hours), has a known history of gastroparesis, is obese, or has other risk factors for aspiration, rapid –sequence induction should be performed. These patients should receive a no particulate antacid. Anesthesiologists should have available all the tools necessary for difficult intubations. After tracheal intubation, general anesthesia is maintained most often with isoflurane, a low-dose narcotic, and a skeletal muscle relaxant. Nitrous oxide may be used concurrently with isoflurane, allowing rapid adjustment of anesthetic depth during any period of potential hemodynamic instability (such as revascularization). Most patients can then be extubated after surgery (15). In addition to the standard anesthetic agents and intravascular fluids, all patients receive broad spectrum antibiotics throughout surgery and low dose (70 units/kg) of intravenous heparin 5 minutes before clamping the major vessels. A variety of immunosuppressive agents (including intravenous prednisolone and azathioprine) are also administered. Cyclosporine may be given as well, but it is often after surgery (13,

22).

**Monitoring (15):**

Standard monitoring includes pulse oximetry, noninvasive blood pressure, esophageal temperature probe, continuous electrocardiography, capnography, and end- tidal gas analysis. In addition, pancreas transplantation patients need central venous pressure monitoring to assess their intravascular volume status and provide central intravenous access for immunosuppressive drugs, inotropic support if required, blood sampling, and hyperalimentation for patients who cannot attain adequate enteric intake. An arterial catheter is placed before anesthesia induction to allow rapid detection of changes in blood pressure. Some recommend pulmonary artery thermo-dilution catheters in all patients with significant cardiac or pulmonary disease. Cardiac output and intravascular volume status can then be optimized before graft perfusion with intravenous fluids, vasodilators, or inotropes (15,23).

**Metabolic Status (11):**

Monitoring metabolic status is important in pancreas transplantation. Serum glucose levels must be checked at least hourly throughout surgery and every half-hour if significant adjustments are made. Glucose determinations should be made every half-hour immediately after allograft reperfusion, both to optimize the glucose level during this critical period and to help determine if the islet cells are functioning (15).

Pancreas recipients often become hyperglycemic from the metabolic response to stress, the reduced effect of insulin during anesthesia and surgery, the hyperglycemic effect of corticosteroids or cyclosporine, and administration of dextrose as a component of urine replacement after renal revascularization (24, 25). Glucagon from the reperfused pancreas allograft may induce hyperglycemia (26). To prevent hyperglycemia, some authors suggest holding dextrose-containing solutions throughout surgery unless the blood sugar level falls below 70 mg/dl. If the patient becomes hyperglycemic even when dextrose is withheld,

insulin may be infused. Hemodynamic status must be optimal before and after perfusion of the pancreas allograft. Reduction in graft flow and the release of thrombosis factors from the transplanted pancreas may result in vascular thrombosis (27). To ensure adequate perfusion and prevent hypotension with reperfusion, patients must have an adequate circulating blood volume when the vascular clamps are released. In younger patients without significant cardiac disease, blood volume can be expanded with normal saline, colloids (e.g., 5% albumin or 6% hetastarch), or packed red blood cells until the central venous pressure is at least 14 mmHg at the time of reperfusion. Hypotension, if it still occurs, may be treated with vasopressors, such as ephedrine, or dopamine (15). Simple volume expansion before reperfusion may not be adequate for patients with serious cardiovascular disease. In such patients, central venous pressure may not be an accurate index of volume status and does not guarantee that cardiac output is adequate for perfusion. Thus, a pulmonary artery catheter should be used. Edema of the pancreas allograft after reperfusion can also cause vascular insufficiency and graft thrombosis. Crystalloid fluid overload should be avoided. An adequate hemoglobin level (10g/dl) must be ensured by including packed red blood cells during fluid expansion before reperfusion.

#### **Postoperative Care (11):**

After surgery, most pancreas recipients can be actuated after reversal of neuromuscular blockade, provided that they are alert and thermodynamically stable. Serum glucose, electrolytes, hemoglobin, and arterial blood gases should be measured when patients arrive in the recovery room. Dextrose and insulin infusions should be maintained in the recovery room and adjusted based on the serum glucose and electrolyte levels (15). Intravenous dextrose infusions should be continued for the patient after discharge from the recovery room. Dextrose and insulin infusions should be maintained in the recovery room and afterwards until patients begin taking adequate nutrition orally, usually within 10

days after surgery. However, patients with poor nutritional status at the time of surgery may benefit from intravenous hyper-alimentation. An insulin infusion is continued if serum glucose levels remain above 150 mg/dl. Patients often require supplemental sodium bicarbonate to treat metabolic acidosis because bicarbonate is lost from the pancreatic secretions into the bladder and urine. Pancreas graft function is assessed by tracking serum glucose and urinary amylase levels. Principles of immunosuppression for pancreas recipients are basically the same as those for other solid organ transplants. The amount of immunosuppression required, however, appears to be more than that of liver, heart, or kidney transplants alone, because of the higher number of pancreas rejection episodes. Rejection is the most common cause of graft failure, accounting for up to 30% of graft losses in the first year after transplantation.

#### **CONCLUSION**

Pancreas transplantation promises to benefit many patients with IDDM, primarily by improving their quality of life and also by possibly preventing some of the secondary complications of disease. Results will continue to be improved with advances in surgical techniques, preoperative care, and immunosuppression.

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