End-stage renal failure in diabetic nephropathy: CAPD vs other approaches

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Continuous ambulatory peritoneal dialysis is an acceptable and comparable alternative to hemodialysis as a renal replacement therapy for end stage renal disease patients. To achieve the goal of adequate dialysis for ESRD patients peritoneal dialysis, an intra-corporeal therapy, makes use of a biological membrane, the peritoneum for dialysis. Peritoneal, not a vascular access is essential for the process. Until the advent of CAPD in late seventies, peritoneal dialysis schedules (like hemodialysis) were repetitive and intermittent. However, CAPD schedules allow for continuous treatment and reduce the problems inherent to all intermittent dialysis therapies such as insuppressible thirst, excessive weight gain and hypertension due to fluid retention in between the dialysis treatments, and hypotensive episodes during the treatment with ultra-filtration. Peritoneal access allows for infusion of intraperitoneal medications such as antibiotics and insulin.

When a patient with diabetic nephropathy approaches the stage of requiring dialysis, he also usually has other target organ damage due to complications of diabetes and premature atherosclerosis. It is not uncommon to see in a diabetic patient all or some of the following complications: crippling coronary artery disease, peripheral vascular disease with ischemic complications, proliferative retinopathy or cerebro-vascular disease. In addition, he may have debilitating autonomic neuropathy with symptomatic orthostatic hypotension. These are challenging patients to care for on any form of dialysis. Any rapid fluctuations in the hemodynamic status of these patient are likely to precipitate acute coronary or cerebro-vascular events. Creating a vascular access for hemodialysis in these patients with hardened arteries is a challenge to any vascular surgeon. Systemic heparinization, required during hemodialysis is alleged to cause bleeding in the retinal tissue which may be undergoing changes of neovascularization due to diabetes.

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Experiences of the past decade with CAPD indicate that this form of dialysis therapy is ideally suited for diabetic patients with end stage renal disease because it is a continuous and slow therapy and is devoid of the rapid fluctuations in biochemical parameters and fluid status seen with the intermittent forms of dialysis therapy. Not having to access a blood vessel and to give heparin are the additional medical benefits of CAPD. Preliminary evidences to be discussed later in this section suggest CAPD preserves residual renal function for a period longer than hemodialysis. Moreover, there are several social and economical benefits which may have impact on a patient's sense of well being such as the opportunity for home dialysis, no need to use machinery, a simple and flexible technique with a short training period, and the free mobility.

Access to peritoneum allows administration of insulin into the peritoneal cavity for blood glucose control. Kinetics of intraperitoneal insulin uptake closely resembles that of insulin uptake once it is released from the pancreas in normal person. Insulin release in a normal person is a complex coordinated interplay of food absorbed from the gut, gastrointestinal hormones and other hormonal and neural stimuli. Pancreatic islets secrete insulin into the portal vein and the liver removes 50 to 60 % of the insulin presented to it. The insulin taken up by the liver inhibits hepatic glycogenolysis, gluconeogenesis, and ketogenesis, and facilitates glycogen and fatty acid synthesis [1]. The insulin secretory rate necessary to maintain normal basal concentrations of insulin is in the range of 0.25 to 1.5 U/h [2]. These basal rates of secretion are normally present in the intervals between meal ingestion. Continuous infusion of insulin, by maintaining a basal level, effectively normalizes blood glucose concentrations in type 1 diabetes than are premeal insulin doses alone [3]. Because of the continuous therapy, CAPD allows for maintenance of basal insulin levels in the blood. Insulin administered into the peritoneal cavity is absorbed by diffusion across the visceral peritoneum into the portal venous circulation and directly through the capsule of liver [4] and thus simulates physiological insulin secretion more closely than systemic insulin therapy [5]. Intra-peritoneal insulin also reaches the systemic circulation by convective transfer via the peritoneal cavity lymphatics [6]. Insulin appears in the serum very rapidly after peritoneal

instillation and is dose dependent [7, 8]. Intraperitoneal administration of regular insulin allows the control of glycemia throughout the dwell time, related most likely to maintaining a basal level of insulin; intraperitoneal insulin is absorbed along with the obligatory glucose load from the dialysis solution and insulin absorption is continuous until the end of the dwell. Peak insulin levels in the serum are observed 30 to 45 minutes after administration into an empty peritoneal cavity [5] and delayed until 90 to 120 minutes when insulin is added to the dialysis solution [9]. Approximately 50 % of the insulin instilled into the peritoneal cavity is absorbed after an 8 hour dwell time [10]. Because of these features, the intraperitoneal administration of insulin during CAPD is more physiological than multiple subcutaneous injections given during intermittent dialysis therapy. Therefore, for diabetics with end stage renal disease, if no contraindications exist, CAPD should be the treatment of choice so that intraperitoneal insulin could be administered.

It is claimed that administration of intraperitoneal insulin would increase the incidence of CAPD related peritonitis because it breaks the sterility of the system and potentially could contaminate the peritoneal cavity [11, 12]. However, clinical experience with larger population has shown the peritonitis incidence to be of no different than in nondiabetics on CAPD [13]. The USA CAPD Registry surveyed peritonitis rates per patient year by route of insulin administration and type of diabetes management [14]. Although the differences in the rates were not large, diabetics never using insulin had the highest rate of peritonitis per patient year (1.31) while patients using a combination of subcutaneous and intraperitoneal insulin experienced the lowest rate (0.93). The peritonitis rate per patient year for patients using subcutaneously administered insulin (1.03) was similar to the rate reported for patients using intraperitoneal insulin (1.06). Blind patients using subcutaneously administered vs blind patients using intraperitoneal insulin reported similar rates of peritonitis. The reason for relatively low peritonitis rates in patients using insulin is unclear; it is being suggested that insulin may have a bactericidad effect. The recent trend has been to use devices meant to facilitate exchange procedures or protect against peritoneal contamination, especially the Y-set system, the introduction of which has significantly lowered the incidence of peritonitis [15]. The clinical manifestations and management of peritonitis in both diabetics and nondiabetic are similar.

Theoretically, CAPD may be associated steady glomerular capillary pressure in the remaining functioning nephron without any fluctuations to high or low levels. Also, blood-membrane interaction during hemodialysis may result in release of interleukins and other mediators of inflammatory responses that may injure remaining glomerular endothelium [16]. These feature of CAPD may have protective effect on patient's residual renal function. A prospective study showed a greater decline in the residual function in patients on hemodialysis (80 %) compared to CAPD (25 %) patients [17]. Based on their large experience, Rottembourg et al [18] recommend "in patients with end stage renal diseases, CAPD should be the treatment of choice when factors such as uncontrolled hypertension, cardiac failure, severe nephrotic syndrome, rapidly progressive renal failure, analgesic or non-steroidal anti-inflammatory drug treatments or abuses. chronic urinary obstruction, or cholesterol emboli are present, expecting a later recovery of renal function". Another cross sectional comparison study of residual renal function in CAPD patients compared to hemodialysis patients found higher endogenous creatinine clearance in CAPD patients compared to hemodialysis patients [19]. These observations are a compelling reason to recommend CAPD therapy for those patients with significant residual renal function or in whom recovery of renal function is anticipated. Preserving the residual renal function has clinical implications for the dialysis prescription, and fluid, sodium and potassium balance during dialysis treatment.

Thus, because of the slow continuous process CAPD is ideally suited for diabetic ESRD patients who invariably have associated diffuse atherosclerotic disease. Additionally, CAPD facilitates intraperitoneal infusion of insulin and may have protective effect on preserving residual renal function.

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