Management of diabetic patients with haemodialysis, peritoneal dialysis, and renal transplantation

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Introduction

More than 30 years ago diabetic patients with end-stage renal disease (ESRD) were considered as inappropriate candidates for a chronic dialysis programme because of a very high mortality rate and poor long-term survival [1]. In spite of this negative attitude against diabetics on dialysis, not only more and more diabetic patients have been accepted to chronic renal replacement therapy, but diabetes has become the most common cause of ESRD, leading to renal replacement therapy in the western world [2]. Although the prognosis has improved markedly, mortality and morbidity are still higher in diabetic compared to non-diabetic patients undergoing haemodialysis (HD), peritoneal dialysis (PD), or after renal transplantation.

Diabetic patients and HD

In diabetic patients HD should be started earlier than in non-diabetic patients usually at a creatinine clearance >15 ml/min. To obtain reliable information about glomerular filtration rate (GFR), both creatinine and urea clearance should be performed to avoid overestimation of the true GFR.

The best vascular access for both non-diabetic as well as diabetic ESRD patients is a native arteriovenous fistula (AVF). Advanced atherosclerosis of the arteries and scarred, stenotic or occluded veins in the forearm make creation of a radiocephalic AVF sometimes difficult if not impossible. Brachiocephalic AVF or transposition of basilic vein AVF is then the vascular access of choice because of good function and a prolonged primary patency rate [3]. Careful duplex sonography of arteries and veins should be performed prior to AVF construction to define the optimal anastomosis site [4]. Ideally, the AVF should be created at a creatinine clearance of 25–35 ml/min in order to have enough time for AVF maturation. When a native AVF cannot be created, arteriovenous graft becomes the second best choice. Ischaemia distally from AVF could be a problem in diabetics, requiring a reduction of blood flow through AVF (by surgical banding) or even its closure.

Bicarbonate HD with 5.5 mmol/l of glucose in the dialysate is standard HD procedure preventing sudden intradialytic hypoglycaemia and enabling efficient and undisturbed insulin therapy.

The most difficult and important task is achieving patient’s ‘dry weight’ and maintaining a fluid balance in order to adequately control volume-related hypertension and thus avoiding heart failure with pulmonary oedema. Almost all diabetic patients are hypervolaemic and hypertensive at the start of dialysis. These patients poorly tolerate excessive ultrafiltration and have a high incidence of hypotension episodes and cramps during HD. Accelerated atherosclerosis and autonomic neuropathy make achieving optimal dry weight difficult. Long, slow dialysis facilitates successful removal of fluid overload: 3 x 8 h of HD in Tassin, France was associated not only with successful removal of excess of body water but was also associated with less hypotension and cramps and with increased survival in both younger as well as older patients [5]. Frequent dialysis or frequent long dialysis should be considered: dialysis as frequent as five times per week was associated with successful fluid removal, with less intradialytic complications and with better quality of life [6]. Overnight dialysis is also becoming more popular.

Antihypertensive therapy in diabetic patients undergoing maintenance chronic HD should be carefully applied: ACE inhibitors block renin-angiotensin-mediated vasoconstriction and, together with atherosclerotic damaged arteries and disturbed sympathetic nerve activity, may dramatically aggravate hypotension episodes during dialysis and thus prevent successful ultrafiltration. Clonidin, calcium antagonists or β-blockers are preferred in overhydrated hypertensive diabetic patients. Intensive and rapid fluid...
removal with or without hypotension results in frequent cardiac arrhythmias and even silent non-transmural myocardial infarctions, contributing to the higher mortality of these patients.

Hypotensive diabetic patients may benefit from on-line haemofiltration or acetate-free biofiltration (lack of acetate specific hypotensive effect).

Heparin as anticoagulant during dialysis is no longer considered as a causative factor of retinal haemorrhage. Furthermore, low molecular weight heparin which is increasingly used in HD procedures, has a favourable effect on lipid profile and might have beneficial effects on accelerated atherosclerosis of diabetic patients. It can also be speculated that the prolonged antithrombotic effects of low molecular weight heparin on dialysis days could have a favourable effect on cardiovascular and cerebrovascular thrombotic events.

**Diabetic patients and PD**

Potential advantages of PD treatment for diabetic patients are the absence of need for vascular access or anticoagulation and the continuity of the procedure with fewer episodes of hypotension, better preserved residual renal function and better control of blood pressure. Anaemia is less pronounced than in HD, the diet is more liberal and patients perform their treatment at home.

Age and co-morbidity are important factors affecting clinical outcome of PD diabetic patients. There is no significant difference in survival between non-diabetic and diabetic patients under the age of 55 years. However, diabetic PD patients over 55 years old have significantly lower survival than non-diabetic patients of the same age. Despite the disparity of results, most medium and long-term studies find no statistically significant differences between overall survival rates of diabetic patients undergoing HD or PD. However, the mortality rate is significantly higher in PD diabetic patients over 55 years old, compared with those on HD. Generally, better survivors are younger with lower body weight, with fewer co-morbidity conditions, have preserved renal function, are in good nutritional state, show low solute transport rates, and have a low incidence of peritonitis [7].

The reduction of peritonitis since late 1980, when the Y-set was introduced, reduced the incidence of dropout from PD and transfers to HD. The main reasons for PD failure are loss of ultrafiltration, malnutrition (peritoneal protein losses are greater in diabetics than in non-diabetics), and peritoneal membrane failure.

**Renal, pancreas, and islet transplantation in diabetic patients**

Kidney transplantation is established as the renal replacement therapy of choice for diabetic patients with ESRD. Pre-transplantation work-up includes additional cardiac evaluation, with some centres requiring coronarography in all diabetics. Regardless of the technique, evaluation of both left ventricular function and coronary arterial supply is necessary [8].

Introduction of chimeric or humanized anti-interleukin-2 receptor monoclonal antibodies (basiliximab or daclizumab) into immunosuppressive protocols, enabling the reduction, withdrawal or even complete avoidance of steroids, seems to be a major step forward for diabetic patients. These monoclonal antibodies are practically free of side-effects. Superior graft survival was demonstrated in diabetics receiving basiliximab compared with placebo [9].

Pancreatic transplantation for type 1 diabetic patients requiring renal transplantation is an important consideration. It can be performed simultaneously with the kidney, which is preferred, or as a pancreas after kidney transplantation procedure [10]. Early results show not only improved patient survival but also long-term kidney graft survival is better after combined organ grafting than after renal transplantation and continuous exogenous insulin [11]. Combined kidney and pancreas transplantation can prevent the progression of diabetic complications and recurrent diabetic nephropathy. In pancreas transplantation alone, even regression of established diabetic nephropathy was observed after 10 years of transplantation [12].

After many years of disappointing results in islet transplantation there was an optimistic report with excellent results in seven patients using a completely steroid-free immunosuppressive protocol consisting of daclizumab, tacrolimus, and sirolimus. Steroid avoidance could have been of crucial importance for this success [13]. Another report of a steroid-free protocol comes from paediatric renal transplantation, this group being at high risk of rejection. This protocol was based on daclizumab, tacrolimus, and mycophenolate mofetil. It seemed that the use of daclizumab in combination with other immunosuppressive agents in both protocols, enabled complete avoidance of steroids, the latter is of particular importance in diabetic patients. There is an interesting hypothesis that lack of any steroid use may obviate a steroid-dependent immune response which makes steroid withdrawal hazardous in renal transplantation.

In the future we can expect further improvement in immunosuppression reducing the side-effects, so that islet transplantation may soon obviate the substantial surgical risk of pancreatic transplantation.

**Conclusions**

Renal transplantation is the treatment of choice for ESRD diabetic patients. In type 1 diabetic patients requiring renal transplantation, simultaneous pancreas transplantation should be considered. In the future we can expect wider use of islet transplantation with new, steroid-free protocols. PD is an attractive option for younger diabetic patients, but for the majority of older patients with late diabetic complications
including impaired vision, haemodialysis still remains the cornerstone of renal replacement therapy.

References

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