Letters to the Editor

Long-Term Subcutaneous Insulin Infusion Therapy and Progression of Nephropathy in Type 1 (Insulin-Dependent) Diabetes

Dear Sir

Diabetic nephropathy is a serious complication of Type 1 (insulin-dependent) diabetes. Once the nephropathy has reached the stage at which the serum creatinine level is raised above normal, renal function usually deteriorates rapidly. We have recorded the length of time taken for serum creatinine to increase from 250 to 500 μmol/l in 32 Type 1 diabetic patients with near-terminal renal failure, who were on conventional long-acting insulin therapy with one or two injections daily. Sixteen patients (50%) had reached a level of 500 μmol/l after 7 months. After 1 year, 26 patients (81%) and after 2 years 31 patients (97%) had serum creatinine levels of 500 μmol/l or more.

We instituted continuous subcutaneous insulin infusion therapy [1] in two male patients with Type 1 diabetes with nephropathy when their serum creatinine level reached 250 μmol/l. Both had a nephrotic syndrome. Microscopy of kidney needle biopsy revealed enlargement of glomerular basement membrane and mesangial matrix. A major proportion (80%) of the glomeruli were destroyed by hyalinization. We used portable Mill Hill 1001 infusers (Muirhead Medical Products, London, UK) and the insulin dosage was adjusted hour by hour so that a situation as close as possible to normoglycaemia was achieved throughout the 24 h. Blood glucose was measured during frequent visits to the hospital and to the local health centre. The patients also checked their own glucose levels with reagent strips and glucometer.

Insulin infusion therapy has continued for 13 months in patient 1 and for 20 months in patient 2 (Table 1). The plasma glucose values obtained by the frequent measurements suggest that a near-normoglycaemic state was achieved in both subjects. Despite this, there was a gradual increase in serum creatinine levels in both patients during the therapy. The rate of the increase in the two patients (mean 6.1 μmol/l per month) was slower ($p < 0.001$; Student's t-test) than in the patients on conventional insulin therapy (mean 39.1 μmol/l per month). Heavy proteinuria (3–10 g/24 h) continued and retinal photocoagulation was necessary in both patients. The patients were on moderate antihypertensive medication which remained unchanged. There was no change in blood pressure during the infusion period (mean for Patient 1: 151/97 mmHg; mean for Patient 2: 167/92 mmHg at the end).

We draw the following conclusions: (1.) Diabetic nephropathy worsened in spite of the dramatic improvement in long-term blood glucose levels, suggesting that the progression of renal microangiopathy, close to the final stages at least, is not solely dependent on long-term blood glucose level. (2.) Comparison of the rate of the serum creatinine increase with the data collected from similar patients on conventional insulin therapy does, however, suggest that the progression of nephropathy may have been considerably slowed in these two patients. (3.) These results have encouraged us to apply the infusion technique to patients with less advanced

Table 1. Plasma glucose, serum creatinine levels and creatinine clearance during continuous insulin infusion treatment in two male patients with Type 1 diabetes, diabetic nephropathy and retinopathy

	Patients	
	1	2
Duration of insulin infusion therapy (months)	13	20
Plasma glucose levels during infusion therapy (mmol/l)	5.6 ± 2.7[a] ($n = 58$)	5.8 ± 2.5[a] ($n = 118$)
Serum creatinine (umol/l)		
Beginning of infusion period	250	250
End of infusion period	295	430
Creatinine clearance (ml/min per 1.73 m^2)		
Beginning of infusion period	43	39
End of infusion period	33	17.5

Patient 1: age 34 years, duration of diabetes 25 years; Patient 2: age 40 years, duration of diabetes 26 years
[a] Results expressed as mean ± SD (n = number of observations)

nephropathy. This will provide further information on the rate of progression of diabetic nephropathy and on its relationship to long-term blood glucose levels [2].

Yours sincerely

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References

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2. Watkins PJ (1980) Insulin infusion systems, diabetic control, and microvascular complications. Br Med J 1: 350–352

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