Ian W Campbell

Benefits of ACE inhibitors in diabetic renal disease: a new era for patients with diabetes

It is difficult to say that any one paper changed my life. When I was asked to write this short commentary, I wondered whether I should choose the first paper describing the role of laser photocoagulation in preventing blindness from diabetic retinopathy because I started my career in diabetes in 1970 when only pituitary ablation was available to prevent the relentless progression of advanced diabetic eye disease to blindness. Perhaps I could have selected the Diabetes Control and Complications Trial (DCCT) or the results from the United Kingdom Prospective Diabetes Study (UKPDS) showing that good glycaemic control has benefits for patients with both type 1 and type 2 diabetes, respectively.

I chose none of these, but rather I opted for the original paper by Lewis et al in 1993, which clearly showed the benefits of angiotensin-enzyme inhibition on diabetic nephropathy (Lewis et al, 1993). I was present at the original oral presentation of this work by Professor Lewis in London and can recall vividly the effects that these results had on me and how these could be translated readily into my own every day clinical practice.

I have been in diabetes medicine since 1970 and a consultant in this speciality since 1978. How many of today's junior doctors training in diabetes (or indeed renal disease) have seen a young patient with type 1 diabetes dying a slow horrible death from uraemia? The sallow pallor of the face, the tired withdrawn look in the eyes, the constant nausea and frequent vomiting and diarrhoea. I recall being called as a resident at 2 am to see a 28-year-old female (I can even remember her name after 34 years: 'Mrs CD'), blind from proliferative diabetic retinopathy, with intractable hiccoughs and vomiting, uraemic 'frost' on the lips, an easily heard pericardial rub and twitching of the muscles in arms and legs – all classical textbook features of chronic renal failure. No dialysis was available. Haemodialysis was considered dangerous in patients with diabetic eye disease and continuous ambulatory peritoneal dialysis (CAPD) was in its infancy. Transplantation was likewise not offered to patients with diabetes. Mrs CD died the following morning.

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The 1980s confirmed that proteinuria and later microalbuminuria were strong predictors of not only renal failure but also of cardiovascular morbidity and mortality in diabetes. Lewis et al showed that captopril therapy over a 3-year period was associated with a 50% reduction in a combined endpoint of death, dialysis and transplantation in patients with type 1 diabetes and proteinuria. It was the first clear demonstration that angiotensin-converting enzyme (ACE) inhibitors gave renal protection.

Following the study by Lewis et al, the benefits of ACE inhibition in preventing the progression of microalbuminuria to proteinuria in patients with type 1 diabetes have been published. Likewise the benefits of ACE inhibitors in diabetic renal disease in type 2 patients have been shown. Similar benefits from the more recently introduced angiotensin receptor antagonists (A11A) have been demonstrated in the IRMA-2 and IDNT studies with irbesartan and in the RENAAL study with losartan (Walker, 2002).

It would be rare to see untreated terminal uraemia in a patient with type 1 diabetes or indeed a patient with type 2 diabetes without end-stage renal failure management being offered. ACE inhibitors or A11As are now used in all patients with diabetes with any degree of nephropathy. Lewis et al in 1993 showed the way. I have not seen any 'Mrs CD' patients in the past decade … but I still remember that night 34 years ago!

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