Efecto del bloqueo del sistema renina angiotensina sobre la progresión de la nefropatía diabética

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Diabetes mellitus is one of the most common diseases worldwide. It has been estimated that the total number of diabetic patients worldwide will increase from 123 million (1997) to 220 million by the Year 2010, with approximately 97% of all diabetics being type 2. Up to 40% of type 2 diabetics develop kidney disease, and in certain geographical regions, approximately 40% of new patients receiving renal replacement therapy have diabetic nephropathy. In the United States, the overall incidence of ESRD continues to increase, while the number of new ESRD cases attributed to diabetes is projected to rise sevenfold by 2030.

Both hemodynamic and non-hemodynamic mechanisms may contribute to the progression of diabetic nephropathy. Since angiotensin II (AII) plays a central role in these mechanisms, it therefore has been hypothesized that blockade of AII would be renal protective in patients with type 2 diabetes.

In experimental models of both non-diabetic and diabetic renal disease, AII receptor antagonism with losartan has been shown to reduce intraglomerular pressure and glomerular sclerosis, and reduce urinary protein excretion. These findings were supported in non-diabetic patients where losartan lowered blood pressure, decreased urinary protein excretion, and elevated renal plasma flow. In type 1 diabetes, ACE inhibition was demonstrated to slow the progression of renal disease, however there was no definitive evidence of a benefit on ESRD in type 2 diabetes.

The RENAAL study was initiated to investigate the long-term renal protective effects of losartan in patients with type 2 diabetes and nephropathy. The study demonstrated that losartan compared to placebo (with or without conventional antihypertensive therapy) significantly reduced the incidence of and delayed the time to the composite outcome of doubling of serum creatinine, ESRD, or death. RENAAL also demonstrated for the first time that blockade of angiotensin II with losartan delayed ESRD and the composite endpoint of ESRD or death. Losartan compared to placebo also significantly reduced proteinuria over time.

The RENAAL study also revealed the association between important risk factors and renal outcomes in this type 2 diabetic population with nephropathy. Baseline metabolic factors were shown to be associated with the composite endpoint as well as ESRD, while anemia was shown to be an independent risk factor for rate of glomerular filtration rate decline and ESRD. Baseline proteinuria also was shown to be an important predictor for renal outcomes in this population. Furthermore, from RENAAL we have learned that imbalances in distribution of baseline proteinuria between treatment groups may affect treatment outcomes in studies of renal diseases.

In summary, the results from the RENAAL study have fulfilled an unmet medical need by providing evidence that AII receptor antagonism is effective in delaying the onset of ESRD in type 2 diabetes, and well-tolerated in this vulnerable population. This study also revealed important information on the predictive nature of certain risk factors for renal outcome in type 2 diabetic patients with nephropathy.