The Role of TNF-alpha in the Progression of Diabetic Nephropathy

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Diabetic nephropathy (DN) is one of the major causes of end stage renal disease. Recent studies suggest that renal inflammation is critical for the development of DN. TNF-alpha is inflammatory cytokine that has been used as a marker and predictor of chronic renal disease. In preliminary studies, we observed that the renal expression of TNF-alpha was elevated in Dahl salt-sensitive (SS) rats with streptozotocin (STZ, type-1 diabetic model). Therefore, the current study examined whether chronic blockade of TNF-alpha with Etanercept (ETN) would prevent the progression of renal injury in STZ-treated SS rats. This study was performed on 9 week-old SS rats which were placed in metabolic cages for a 24hr-urine collection to determine baseline protein excretion. Blood samples were also taken from the tail for the measurement of glucose levels. Then, the rats were injected with STZ (50 mg/kg, i.p.) and protein excretion was measured every 3 weeks until 9 weeks of diabetes was completed. After 3 weeks of diabetes (3 weeks post STZ injection), rats were divided into two treatment groups: (1) vehicle and (2) ETN (0.8 mg/kg twice a week, s.c.) and treated for 6 weeks. After 3 weeks of diabetes, protein excretion increased from 78±5 to 234±46 mg/day. Treatment with ETN reduced protein excretion by 20%. Administration of ETN had no effect on glucose levels and the values were similar to those obtained from vehicle-treated diabetic SS rats. These data indicate that ETN may be a beneficial therapy for the progression of DN.

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