Biocell 2017, 41(1): 1-12

Tubulointerstitial injury and proximal tubule albumin transport in early diabetic nephropathy induced by type 1 diabetes mellitus.

Maximiliano Giraud-Billoud, Fernando Ezquer, Javiera Bahamonde y Marcelo Ezquer

Abstract

A decrease in the tubular expression of albumin endocytic transporters megalin and cubilin has been associated with diabetic nephropathy, but there are no comprehensive studies to date relating early tubulointerstitial injury and the effect of the disease on both transporters in type 1 diabetes mellitus (T1DM). We used eight-week-old male C57BL/6 mice divided into two groups; one of them received the vehicle (control group), while the other received the vehicle + 200 mg/kg streptozotocin (T1DM). Ten weeks after the injection, we evaluated plasma insulin, enzymuria, urinary vitamin D-binding protein (VDBP), tubulointerstitial fibrosis and proximal tubule histology, markers of autophagy, and megalin and cubilin levels. We found a reduction in tubular protein reabsorption (albumin and VDBP as specific substances carried by both transporters) with increased tubulointerstitial injury, development of fibrosis, thickening of tubular basement membrane, and an increase in tubular cell metalloproteases.

This was associated with a decrease in the renal expression of megalin and cubilin. We also observed an increase in the amount of cellular vesicles of the phagocytic system in the tubules, which could be linked to an alteration of normal intracellular trafficking of both receptors, thus affecting the normal function of transporters in early stages of diabetic nephropathy. In diabetic animals, the added effects of tubulointerstitial injury, the decreases in megalin and cubilin expression, and an altered intracellular trafficking of these receptors, seriously affect protein reabsorption.