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Renal GLUT1 reduction depends on angiotensin-converting enzyme inhibition in diabetic hypertensive rats

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Abstract

Aims

Angiotensin-converting enzyme (ACE) inhibitors are used in diabetic kidney disease to reduce systemic/intra-glomerular pressure. The objective of this study was to investigate whether reducing blood pressure (BP) could modulate renal glucose transporter expression, and urinary markers of diabetic nephropathy in diabetic hypertensive rats treated with ramipril or amlodipine.

Main methods

Diabetes was induced in spontaneously-hypertensive rats (~ 210 g) by streptozotocin (50 mg/kg). Thirty days later, animals received ramipril 15 μg/kg/day (R, n = 10), or amlodipine 10 mg/kg/day (A, n = 8,) or water (C, n = 10) by gavage. After 30-day treatment, body weight, glycaemia, urinary albumin and TGF-β1 (enzyme-linked immunosorbent assay) and BP (tail-cuff pressure method) were evaluated. Kidneys were removed for evaluation of renal cortex glucose transporters (Western blotting) and renal tissue ACE activity (fluorometric assay).

Key findings

After treatments, body weight ($p = 0.77$) and glycaemia ($p = 0.22$) were similar among the groups. Systolic BP was similarly reduced ($p < 0.001$) in A and R *vs.* C (172.4 ± 3.2; 186.7 ± 3.7 and 202.2 ± 4.3 mm Hg; respectively). ACE activity (C: 0.903 ± 0.086; A: 0.654 ± 0.025, and R: 0.389 ± 0.057 mU/mg), albuminuria (C: 264.8 ± 15.4; A: 140.8 ± 13.5 and R: 102.8 ± 6.7 mg/24 h), and renal cortex GLUT1 content (C: 46.81 ± 4.54; A: 40.30 ± 5.39 and R: 26.89 ± 0.79 AU) decreased only in R ($p < 0.001$, $p < 0.05$ and $p < 0.001$; respectively).

Significance

We concluded that the blockade of the renin–angiotensin system with ramipril reduced early markers of diabetic nephropathy, a phenomenon that cannot be specifically related to decreased BP levels.

Keywords

Angiotensin-converting enzyme inhibitors; Diabetes mellitus; Diabetic nephropathy; Glucose transporter proteins; Hypertension; Streptozotocin

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