

Interactions between Renin Angiotensin System and Advanced Glycation in the Kidney

Merlin C. Thomas, Christos Tikellis, Wendy M. Burns, Katarzyna Bialkowski, Zemin Cao, Melinda T. Coughlan, Karen Jandeleit-Dahm, Mark E. Cooper, and Josephine M. Forbes
Baker Medical Research Institute, Melbourne, Victoria, Australia

Although hemodynamic and metabolic factors are individually implicated in the development of diabetic nephropathy, their interaction has not been defined clearly. In this study, the effects of angiotensin II (Ang II) and advanced glycation end products (AGE) both individually on each other are explored and compared. In the first study arm, Sprague-Dawley rats received a continuous infusion of AGE-modified rat serum albumin (RSA) or unmodified RSA for 4 wk with or without the angiotensin receptor type 1 antagonist valsartan. In the second arm, animals received a continuous infusion of Ang II (58.3 ng/kg per min) with or without the AGE inhibitor pyridoxamine. Components of the intrarenal renin-angiotensin system were measured using real time reverse transcription-PCR, immunohistochemistry, and standard angiotensin-converting enzyme (ACE) activity assays. Renal and serum AGE were quantified by immunohistochemistry, ELISA, and AGE-fluorescence. After an infusion of AGE-RSA, renal expression of angiotensinogen, ACE, renin, and angiotensin receptor type 1 were increased significantly (all $P < 0.01$), and ACE activity was elevated. This was associated with tubular and glomerular hypertrophy and AGE accumulation, which could be antagonized by valsartan. However, valsartan had no effect on increased filtration fraction associated with an AGE-RSA infusion. At the same time, an infusion of Ang II increased the serum and renal accumulation of AGE and advanced oxidation protein products and induced renal hypertrophy and salt retention that could be antagonized by pyridoxamine. However, pyridoxamine had no effect on renal vasoconstriction manifested by reduced renal blood flow. AGE and Ang II have overlapping activities in the kidney. The beneficial effects of blockade of either pathway underline the importance of this interaction in diabetic renal disease and the aging kidney.

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