Angiotensin- Insulin cross talk - A true translational story from bedside to bench

Sharma S Prabhakar

Texas Tech University Health Sciences Center, USA

Abstract

Activation of renin angiotensin aldosterone system (RAAS) has been traditionally incriminated in systemic hypertension and cardiovascular disease and inhibitors of RAAS have been successfully used for over two decades in management of these conditions. Additionally insulin resistance underlies most patients with essential hypertension. Arterial hypertension is an insulin-resistant condition associated with increased cardiovascular and renal morbidity and mortality. Of specific importance in this context, was the unanticipated outcome of primary prevention of diabetes in a number of large scale clinical trials that used RAAS inhibitors. This interesting observation led to intense investigation into the interaction of angiotensin and insulin signaling systems. Evidence from these clinical trials as well from experimental models of insulin resistance including our findings in ZSF rat model will be presented. Recent developments in this field as well as the current understanding of the clinical implications of the cross talk between the insulin and angiotensin signaling systems are the focus of this presentation. One segment of this lecture deals specifically with the discussion of the cellular mechanisms of angiotensin action which interface with insulin signaling in the context of arterial hypertension. In another part, I will discuss the experimental evidence that point to multiple stages in the insulin signaling that are affected by angiotensin blockade which could contribute to improved insulin sensitivity. Angiotensin II inhibits insulin signaling by JNK and MAPK-mediates serine phosphorylation of the insulin receptor, IRS-1 and PI 3-kinase. Drugs acting on angiotensin II generation and signaling have a beneficial effect on hypertension and on type 2 diabetes mellitus prevention. Implications to potentially develop new preventive and therapeutic strategies will also be discussed. Unraveling the mechanistic details of such interaction opens up new opportunities to develop innovative preventive and therapeutic strategies in insulin resistant states and metabolic syndrome.

Biography

Sharma Prabhakar is a distinguished nephrologists and physician scientist currently at Texas Tech University Health Sciences Centre, where he is a tenured professor in the Departments of Medicine and Cell Physiology & Molecular Biophysics and the Chief of Nephrology Division and Vice Chairman, Department of Medicine. He is an established researcher examining pathophysiologic mechanisms of diabetic nephropathy and of insulin resistance in vitro and animal models. In the area of clinical research he initiated and is the principal investigator of a number of clinical studies. Dr Prabhakar has over 100 publications including original articles, reviews, book chapters and published abstracts in prestigious journals such as the American Journal of Physiology, Journal of American Society of Nephrology, and Kidney International. He has recently published a reference book on "Advances in the pathogenesis of diabetic nephropathy" and a two volume reference book entitled "Glomerulopathies". In recognition of his excellence in practice of medicine, Dr Prabhakar was awarded an endowed chair by the University Medical Center. He is active in several professional societies and organizations and is the current President of American Federation for Medical Research.