

23rd International Conference on

HERBAL AND ALTERNATIVE REMEDIES FOR DIABETES AND ENDOCRINE DISORDERS

November 02-04, 2017 Bangkok, Thailand



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Recent progress for the treatment of diabetic nephropathy

In Japan, diabetic nephropathy is the leading cause requiring dialysis since 1998. The number of patients under dialysis is about 320,000, 40% of which are diabetics. Since dialysis costs expensive, prevention of the progression of diabetic nephropathy is an urgent target. We evaluated the incidence of diabetic nephropathy (macroalbuminuria of more than 300 mg/g.Cre) from normo- and low-microalbuminuria (<150 mg/g.Cre) in 1550 type-2 diabetics during 8 years. The onset of macroalbuminuria was observed in 0.67% of the patients, which was one third of the incidence reported in UKPDS. Moreover, 30% of patients with low-microalbuminuria returned to normoalbuminuria (remission/regression). The higher the initial albuminuria, HbA1c, or systolic blood pressure was; the progression risk to macroalbuminuria was higher. Smoking was also the risk for diabetic nephropathy. There were many trials which elucidated the effectiveness of ACE inhibitors or ARBs (angiotensin II receptor antagonists) including ours such as Japan IDDM, INNOVATION, ORIENT and ROADMAP study. However, relative risk reduction with these RAS inhibitors was about 20-30% in patients with macroalbuminuria and 60% in patients with microalbuminuria. We need more vigorous strategy to prevent the new onset and/or progression of diabetic nephropathy. Recent trials using SGLT2 inhibitors such as empagliflozin or canagliflozin decreased not only cardiovascular outcomes by 14% but also renal outcomes by 30-40%. SGLT2 inhibitors may increase sodium delivery to the macula densa and then improve TubuloGlomerular (TG) feedback, which may result in constriction of afferent arteriole and hence amelioration of hyperfiltration. DPP-4 inhibitors and GLP-1 receptor antagonists may have such an action as well. These new hypoglycemic agents may have a great potential to protect renal functions, especially diabetics with hyperfiltration. Furthermore, we are waiting new renoprotective drugs such as anti-oxidant Nrf2 stimulator, bardoxolone methyl or non-steroidal Mineralocorticoid Receptor Antagonist (MRA), finerenone.

Biography

Shigehiro Katayama has been the Director of Saitama Medical University Hospital since 2008 and the Deputy Head from 2002 to 2008. He is currently Director of Saitama Medical University Kawagoe Clinic since 2014. He also has been the Professor and the Head of Endocrinology and Diabetes Division at Faculty of Medicine, Saitama Medical University since 1995 and retired to be Emeritus Professor in 2015. He has graduated from Faculty of Medicine, The University of Tokyo and received MD degree in 1973 and PhD degree in 1980 from The University of Tokyo. He was Postdoctoral Research Fellow at the Rockefeller University in 1980 and Assistant Professor at the State University of New York at Buffalo from 1981-1983. He moved to Saitama Medical University in 1983. His research interests are in hypertension in diabetics in relation to effects of hypoglycemic and/or hypotensive agents on insulin resistance and in relation to diabetic nephropathy. He is a board certified Member of Japanese Society of Internal Medicine, Japan Endocrine Society, Japanese Society of Nephrology, Japanese Society of Hypertension, Japanese Society of Diabetes and a Fellow of American Diabetes Association, American Heart Association (High Blood Pressure Council). He has also received Expert Investigator Award from the Japanese Society of Diabetic Complications in 2012 and Society Award from the Japanese Society of Hypertension in 2013.

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