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Possible mechanisms of action of glucagon-like peptide-1 receptor agonists on blood pressure beyond body weight

Glucagon-like petide-1 (GLP-1) increases insulin and decreases glucagon secretion from the pancreas reacting to nutrient ingestion. Becuase a plasma half-life of native GLP-1 is short, several synthesized GLP-1 receptor agonists (RAs) were innovated for the treatment of type 2 diabetes mellitus (DM). In clinical trials, GLP-1 RAs were shown to significantly reduce blood pressure (BP) besides HbA1c and body weight (BW), suggesting the potential as anti-hypertensive medication of individuals with type 2 DM. Although the hypotensive effect of GLP-1 RAs seems to be caused by BW reduction, other mechanisms other than BW reduction could be implied by the results of mediation meta-analysis, which suggests an involvement of BW-independent hypotensive effect of GLP-1 RA, along with the clinical evidences of weak or no correlations, and different time-course between BP lowering and BW reducing effects. Both human and animal studies demonstrated inconsistent BP response to acute administration but showed hypotensive effect of chronic administration of GLP-1/ GLP-1 RAs. Enhancement of natriuresis by inhibiting sodium hydrogen exchanger at renal proximal tubules or alleviating angiotensin II activity, and stimulation of vasodilation can be recognized as possible mechanisms of hypotensive effect beyond BW. In 2003, we proposed “ Metabolic Domino”, which illustrates time-course of the whole picture of metabolic syndrome, that is, the cause, phathophysiology and complications. Since GLP-1 RAs exert three beneficial actions, that are glucose, BW and BP lowering, they are highly expected to exert potent and coordinated effects for combating Metabolic Domino.

Keywords: hypertension, diabetes mellitus, obesity, metabolic syndrome, glucagon-like petide-1, Metabolic Domino

Biography

Hiroshi Itoh was the professor of Department of Endocrinology, Metabolism and Nephrology, Keio University School of Medicine, Tokyo, Japan and was the president of Japanese Society of Hypertension, Japan Endocrine Society, and Japanese Society of Cardiovascular Endocrinology and Metabolism. He received Takamine Jokichi Award, Expert Investigator Award of Japanese Society of Diabetic Complications, Imura Clinical Research Award, Japan Endocrine Society Award and Japanese Society of Hypertension Honorary Award. His research interests include hypertension, diabetes mellitus, metabolic syndrome, cardiovascular hormones, diabetic nephropathy and longevity medicine.

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