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***Hiroshi Itoh, Masami Tanaka**

HI: Specially-appointed Professor, Center for Preventive Medicine, Keio University, Tokyo, Japan

MT: Midtown Clinic East, Tokyo Japan

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

Glucagon-like peptide-1 (GLP-1) increases insulin and decreases glucagon secretion from the pancreas reacting to nutrient ingestion. Because 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, pathophysiology 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 peptide-1, Metabolic Domino

Biography

Masami Tanaka is working at the Midtown Clinic East, Tokyo, Japan as Acting Director, after working at the Department of Medicine, Tokyo Women's Medical University, Tokyo, Japan as Associate Professor. Before that, he worked at the Department of Endocrinology, Metabolism and Nephrology, Keio University School of Medicine with the presenting author, Hiroshi Itoh. His research interests include hypertension, diabetes, metabolic syndrome, nephrology and endocrinology. He has been conducted many clinical studies concerning hypertension, diabetes and dyslipidemia. At present, he is interested in pre-emptive medicine and education for medical staff and individuals with diabetes mellitus.