

Incretin-based therapeutics in the management of type 2 diabetes: From Asian perspectives

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The global epidemic of diabetes is a serious medical and social problem in all parts of the world including East and Southeast Asia, which have the highest prevalence of the disease. Type 2 diabetes in East and Southeast Asia is characterized primarily by non-obese and β -cell dysfunction; the pathological manifestation in Europe and North America is generally insulin resistance with obesity. These differences have an immense impact on anti-diabetes prevention and treatment strategies in different populations. Incretin-based anti-diabetic strategies including DPP-4 inhibitors (DPP4i) and GLP-1 receptor agonists (GLP-1RA) have been gaining much attention in the management of type 2 diabetes across Asia. The incretins GIP and GLP-1 are released from the gut in response to dietary nutrients stimulate insulin secretion in a glucose-dependent manner. Meta-analyses of clinical trials on DPP4i and GLP-1RA have found the drugs to be more effective in Asian patients, likely due to amelioration of β -cell dysfunction by incretins. We have recently found a potential link between dietary habits and efficacy of DPP4i. The HbA1c-lowering effect of DPP4i is attenuated by intake of saturated fats (SF), possibly because SF enhance GIP secretion and facilitate fat deposition in collaboration with GIP. Since SF consumption is less in Asia in general compared to Europe and North America, the greater efficacy of DPP4i in Asians may therefore be partly due to dietary habits. We also succeeded in establishing incretin-based diet therapy focusing on meal sequence that ameliorates postprandial glucose elevation often found in Asians. Eating fish before rice was found to enhance GLP-1 secretion and ameliorate postprandial glucose excursion by increasing insulin secretion and delaying gastric emptying, compared to eating fish after rice. Similar reversal of rice and meat, which is rich in SF that enhance not only GLP-1 but also GIP, had similar beneficial effects but facilitated fat accumulation. Thus, the meal sequence, fish before rice, might also enhance HbA1c-lowering effects of DPP4i. In this lecture phenotype of Asian type 2 diabetes and anti-diabetes strategies for Asian type diabetes will be discussed from incretin perspectives.