Pro and Contra of Incretin therapy in Type 2 diabetes

Dario Rahelić

Department of Endocrinology, Diabetes and Metabolic Disorders, Dubrava University Hospital, Zagreb, Croatia

Corresponding author: dario.rahelic@gmail.com

Abstract

Incretins are group of gastroinestinal hormones involved in glucoregulation. Two main hormones involved in glucoregulation are glucagon-like peptide-1 (GLP-1) and gastric inhibitory peptide or glucose-dependent insulinotropic polypeptide (GIP). Both are rapidly inactivated by the enzime dipeptidyl peptidase-4 (DPP-4). Incretin based therapies include GLP-1 receptor agonists and DPP-4 inhibitors. Their main mechanisms of actions are to increase insulin and inhibit glucagon secretion, reduce gastric emptying and reduce food intake. Positive effects on glycemia without hypoglycemia and weight gain are their main advantages. Direct cardiovascular effects of GLP-1 receptor agonists are also documented. Concerns have been raised that incretin based therapies were associated with an increased risk of pancreatitis and pancreatic cancer. Recent trials do not support the hypothesis. Preclinical studies in animals have suggested that incretin based therapies could be associated with thyroid C-cell cancer. However, it was not found in humans. Recent trial of one DPP-4 inhibitor suggested increased risk for hospitalization due to heart failure. Further studies are required. Several large clinical trials are in progress. In presentation *pro et contra* of incretin based therapies will be presented.

The practical issues in Type 2 diabetes management - pharmacogenomic consideration

Sabina Semiz

Department for Biochemistry and Clinical Analysis, Faculty of Pharmacy, University of Sarajevo, Bosnia and Herzegovina

Corresponding author: sabinasemiz@hotmail.com

Type 2 diabetes (T2D) is a complex disease that has a significant potential for stratification in its management, including genetic etiology, treatment outcomes, rate of progression, and development of complications. In the light of exorbitant and still increasing costs of treating T2D and its complications, pharmacogenomics' benefit of selecting patients and adequate therapies offers a considerable potential to improve cost-effectiveness of drug therapy and avoid extra costs for side - effects treatment. Several classes of oral antidiabetic drugs (OAD) are currently available to treat T2D patients, with sulphonylureas (SU), biguanides, thiazolidinediones (TZD), and meglitnides being the most frequently used. Emerging evidence has recently demonstrated that genetic variation might be one of the key determinants of an individual's responses to OAD. A variety of approaches can be used to understand OAD's pharmacodynamic and pharmacokinetic mechanisms related to interindividual differences in drug response, with pharmacogenomics providing a unique and powerful clinically relevant tool. Furthermore, an enhanced understanding of genes and pathways that determine OAD response has also the potential to reveal new drug targets and develop novel drugs for the treatment of diabetes.

Although benefits from a personalized diabetes care are well established in patients with certain monogenic forms of diabetes, pharmacogenomics of common T2D is also anticipated and progressing rapidly. Here are summarized the results of the several recent studies, which have analyzed an association of genetic variations in drug - metabolizing enzymes (DME), drug transporters (DT),