Fall 2014

Incretin Hormones and their effects in Type 2 Diabetes

Molly Getz
Otterbein University, mollygetz@almostfamily.com

Follow this and additional works at: https://digitalcommons.otterbein.edu/stu_msn

Part of the Endocrine System Diseases Commons, Medical Pathology Commons, and the Nursing Commons

Recommended Citation
Getz, Molly, "Incretin Hormones and their effects in Type 2 Diabetes" (2014). Master of Science in Nursing (MSN) Student Scholarship. 39.
https://digitalcommons.otterbein.edu/stu_msn/39

This Project is brought to you for free and open access by the Student Research & Creative Work at Digital Commons @ Otterbein. It has been accepted for inclusion in Master of Science in Nursing (MSN) Student Scholarship by an authorized administrator of Digital Commons @ Otterbein. For more information, please contact shickey@otterbein.edu.
Type 2 diabetes mellitus (T2DM) is a progressive disease characterized by impaired pancreatic β-cell dysfunction, insulin resistance and hyperglycemia (Stephens, 2010, p. 491). T2DM affected 291 million Americans or 9.5% of the population in 2014 (American Diabetes Association, 2015), with many of these patients finding it difficult to achieve or maintain adequate glycemic control. The main challenges and pharmacologic interventions are discussed as follows.

### Disease Management of T2DM

Proper treatment is necessary for patients, including medication therapy, education and active involvement of the patient, with the goal of therapy to lower the A1C (Bartol, 2012). Incretin mimetics are a class of medications available for treating patients with T2DM; they mimic the action of incretins in vivo released during nutrient absorption (Freeman, 2012). Patients with T2DM have an impaired incretin response (Pratley, n.d., p. 8).

#### Incretin Effect

The incretin effect is the secretion of insulins after ingestion of food correlated with the improvement in postprandial glucose levels (Ahren, 2013). Incretins are peptide hormones that originate in the gut and increase the effectiveness of insulin secretion after meal ingestion in a glucose-dependent manner (Drucker, 2013). Glucose-dependent hormones are incretin-like polypeptides (GLP-1) and glucose-dependent rodent insulinotropic polypeptide (GIP). Incretin analogs are lowering glucose levels (Ahren, 2013), and they were associated with a low risk of adverse events related with hypoglycemia (Ahren, 2013).

#### GLP-1

GLP-1 is produced in enteroendocrine cells in the distal small bowel and colon in L-cells (Drucker, 2013, p. 155) and binds to a 5α-protein coupled receptor to the endocrine pancreas (Burgmaier, Heinrich, & Marx, 2012). Via stimulation of adenylate cyclase and cyclic adenosine monophosphate (cAMP) production (Burgmaier et al., 2012, p. 290), GLP-1 increases insulin secretion from pancreatic β-cells and inhibits glucagon secretion from α-cells, increases insulin synthesis, lowers glucose sensitivity to glucose-nonsensitive β-stimulates cell proliferation and regeneration, and increases GIP cell apoptosis (Burgmaier & Drucker, 2013).

GLP-1 plasma levels rise within minutes after food intake and have a short half-life of two minutes and like insulin is degraded rapidly by DPP-4 and excreted via the kidneys (Drucker, 2011). GLP-1 lowers blood sugar levels and body weight by inhibiting appetite by enhancing satiety through hypothalamic action and by slowing gastric emptying, which results in a decreased influx of glucose into the circulation (Pratley, n.d., p. 8).

#### DPP-4

According to Drucker (2006, p. 154), both GLP-1 and GIP stimulate glucose-dependent insulin secretion via activation of their specific G protein-coupled receptors expressed directly on β-cells and β-cells. Both hormones stimulate islets immediately after ingestion of nutrients to increase pancreatic β-cell mass and protect against β-cell cell apoptosis (Vild Hopkins & Knopp, 2014, p. 2).

Incretin-based therapies are used as an add-on therapy to conventional T2DM treatment improving glycemic control in generally well tolerated (Capaldi, 2012). Two classes of incretin-based therapies are DPP-4 inhibitors and GLP-1 receptor agonists.

DPP-4 is the key enzyme responsible for inactivating GLP-1 and GLP-4 and exists in two principal forms: a membrane anchored, large extracellular protein capable of stimulating intracellular signal transduction pathways independent of its enzymatic activity, and a circulating soluble enzyme which retains enzymatic activity (Drucker, 2006, p. 156). According to Drucker (2006), genetic evidence supports an essential role of DPP-4 in the control of glucose homeostasis. DPP-4 inhibitor blocks the action of the enzyme that degrades GLP-1 by slowing the degradation of GLP-1 to the metabolite GLP-1 (9-36) amide (Burgmaier et al., 2012, p. 290). GLP-4 inhibitors also decrease the degradation of other peptides that are substrates to DPP-4, including GIP and a variety of angiotensins (Burgmaier et al., 2012, p. 290).

According to Capaldi (2012), GLP-1 receptor agonists and DPP-4 inhibitors reduce glucose levels with low risk of hypoglycemia. GLP-1 receptor agonists are associated with weight loss, whereas DPP-4 inhibitors are weight neutral (Capaldi, 2012). DPP-4 inhibitors are rapidly absorbed and excreted by the kidney, therefore renal function should be assessed before their use (Aye & Jonesing, 2009, p. 197).

### References

Ahren, B. (2013). The biology of incretin hormones and how they are responsible for the so-called “incretin effect” (Campbell & Drucker, 2012, p. 79). GLP-3 and GLP play an essential role in maintaining normal glucose homeostasis and in particular, postprandial glucose levels (“Incretin Effect,” 2013). Incretins are associated with a low risk of adverse events related with hypoglycemia (Ahren, 2013).