Journal of Diabetes and Metabolism
ISSN: 2155-6156
Shehata and Pater, J Diabetes Metab 2011, 2:7
DOI: 10.4172/2155-6156.1000146
Short Communication
Open Access

Incretin-Based Therapies: What Do We Need To Know?

Marlene F. Shehata[1]* and Alan Pater[2]

[1]*Pharmaceutical Services, Southwestern Ontario, 1102-330 Talbot Street, St. Thomas, ON, N5P 4E1, Canada*
[2]*Memorial University of Newfoundland, Canada*

Short Communication

According to the Canadian Diabetes Association, 2.7 million Canadians (~7.6% of population) were affected with diabetes in 2010 and these numbers will potentially rise to 4.2 million (~10.8% of population) in 2020 demonstrating the need to better control diabetes progression and ultimately lower the above statistics [1] (http://www.diabetes.ca/documents/get-involved/WEB_Eng.CDA_Report_.pdf).

It is essential to note that the progressive nature of type 2 diabetes requires the combination of life style modification (diet and exercise) and antihyperglycemic agents in order to achieve adequate glycemic control [2]. Recently, two therapeutic classes were introduced to the Canadian market to modulate incretin hormones (hormones released in the intestine in response to food intake) [3]. These two therapeutic classes are the glucagon-like peptide 1 (GLP-1) analogues and the dipeptidyl peptidase-4 (DPP-4) inhibitors, which are the focus of the present communication.

To date, two GLP-1 analogues are approved for use in Canada: liraglutide (victoza™ by Novo Nordisk) and exenatide (byetta™ by Eli Lilly). Similarly, two DPP-4 inhibitors are currently in use in Canada: saxagliptin (onglyza™ by Bristol-Myers Squibb Company and AstraZeneca) and sitigliptin (januvia™ by Merck Frosst). Both GLP-1 analogues and DPP-4 inhibitors stimulate insulin secretion, inhibit glucagon secretion in a glucose-dependent manner [4,5] and have a low risk of hypoglycaemia [6].

GLP-1 analogues differ from normal natural GLP-1 in that they are resistant to degradation by DPP-4 and therefore they have longer half life(s) (hours versus minutes) [7]. Distinctive features of GLP-1 analogues include their ability to induce significant weight loss (approximately 3 kg in a patient concurrently taking sulfonylurea or metformin) by suppressing food intake and gastric emptying [8]. GLP-1 analogues improve systolic blood pressure and lipid profiles with superior efficacy to liraglutide over exenatide [6]. Nausea is the most common adverse effect with GLP-1 therapy and is reported in exenatide therapy more than in liraglutide therapy [6]. GLP-1 analogues are administered as subcutaneous injections (liraglutide 0.6-1.8 mg once daily without regards to meals, while exenatide is administered in 5-10 µg doses twice daily at anytime within the 60 minutes prior to the morning and evening meals).

DPP-4 inhibitors, on the other hand, prevent the degradation of endogenous incretins such as GLP-1, and thereby potentiate their actions [7]. DPP-4 inhibitors are very well tolerated weight-neutral medications that are taken orally once daily without regards to food (saxagliptin 5 mg once daily and sitagiptin 100 mg once daily).

Both GLP-1 analogues and DPP-4 inhibitors are used as monotherapy or in combination with metformin alone or together with sulfonylureas in patients with type 2 diabetes who do not achieve adequate glycemic control. GLP-1 agonists if used as monotherapy lower A1C by 1% [9], while DPP-4 inhibitors monotherapy decreases A1C level by 0.7-1% [10]. When GLP-1 analogues are added to metformin therapy, an additional 0.4-0.8% reduction in A1C occurs with exenatide [6] and an additional 1-2% reduction in A1C occurs with liraglutide [11]. On the other hand, when DPP-4 inhibitors are added to the maximum tolerated dose of metformin, an additional 0.78% further reduction in A1C is achieved [12].

In conclusion, despite the better tolerability of DPP-4 inhibitors, GLP-1 analogues are superior in achieving significant weight loss and lower A1C levels. Of the GLP-1 analogues, liraglutide demonstrated superior efficacy, less nausea and less hypoglycaemia with once daily dosing.

References

1. Canadian Diabetes Association. Diabetes: Canada at the tipping point - charting a new path.
2. Bhattacharyya OK, Estey EA, Cheng AY, Canadian Diabetes Association 2008 (2009) Update on the canadian diabetes association 2008 clinical practice guidelines. Can Fam Physician 55: 39-43.
3. Baggio LL, Drucker DJ (2007) Biology of incretins: GLP-1 and GIP. Gastroenterology 132: 2131-2157.
4. Garber AJ (2010) Incretin-based therapies in the management of type 2 diabetes: Rationale and reality in a managed care setting. Am J Manag Care16: 187-194.
5. Jellinger PS (2011) Focus on incretin-based therapies: Targeting the core defects of type 2 diabetes. Postgrad Med 123: 53-65.
6. Shomali M (2011) Add-on therapies to metformin for type 2 diabetes. Expert Opin Pharmacothe 12: 47-62.
7. Siddiqui NI (2009) Incretin mimetics and DPP-4 inhibitors: New approach to treatment of type 2 diabetes mellitus. Mymensingh Med J 18: 113-124.
8. Pratley R, Nauck M, Bailey T, Montanya E, Cuddihy R, Filetti S, et al. (2011) One year of liraglutide treatment offers sustained and more effective glycaemic control and weight reduction compared with sitagliptin, both in combination with metformin, in patients with type 2 diabetes: A randomised, parallel-group, open-label trial. Int J Clin Pract 65: 397-407.
9. Nauck M, Frid A, Hermansen K, Shah NS, Tankova T, Mitha IH, et al. (2009) Efficacy and safety comparison of liraglutide, glimepiride, and placebo, all in combination with metformin, in type 2 diabetes: The LEAD (liraglutide effect and action in diabetes)-2 study. Diabetes Care 32: 84-90.
10. Phung OJ, Scholle JM, Talwar M, Coleman CI (2010) Effect of noninsulin antidiabetic drugs added to metformin therapy on glycemic control, weight gain, and hypoglycemia in type 2 diabetes. JAMA 303: 1410-1418.

***Corresponding author:** Dr. Marlene F. Shehata, R.Ph, BSc. Pharm, MSc. Med., PC., PhD., Clinical Pharmacist, Consultant/Cardiovascular Geneticist, Marlene Shehata Pharmaceutical Services, Southwestern Ontario, 1102-330 Talbot Street, St. Thomas, ON, N5P-4E1, Tel: 519-702-5476; Fax: 347-710-5234; E-mail: marlenefouad@yahoo.com

Received August 26, 2011; **Accepted** September 22, 2011; **Published** October 14, 2011

Citation: Shehata MF, Pater A (2011) Incretin-Based Therapies: What Do We Need To Know? J Diabetes Metab 2:146. doi:10.4172/2155-6156.1000146

11. Buse JB, Rosenstock J, Sesti G, Schmidt WE, Montanya E, Brett JH, et al. (2009) Liraglutide once a day versus exenatide twice a day for type 2 diabetes: A 26-week randomised, parallel-group, multinational, open-label trial (LEAD-6). Lancet 374: 39-47.

12. Grossman S (2009) Differentiating incretin therapies based on structure, activity, and metabolism: focus on liraglutide. Pharmacotherapy 29: 25S-32S.