2016

Impact of Increasing GLP-1 on Markers of Inflammation, Glucose Control and Cardiovascular Risk Factors in Patients With Type 2 Diabetes

Kristina Sandstedt  
*University of North Dakota*

Follow this and additional works at: [https://commons.und.edu/pas-grad-posters](https://commons.und.edu/pas-grad-posters)

Part of the [Cardiovascular Diseases Commons](https://commons.und.edu/cardiovascular-diseases-commons) and the [Endocrinology, Diabetes, and Metabolism Commons](https://commons.und.edu/endocrinology-diabetes-metabolism-commons)

Recommended Citation
Sandstedt, Kristina, "Impact of Increasing GLP-1 on Markers of Inflammation, Glucose Control and Cardiovascular Risk Factors in Patients With Type 2 Diabetes" (2016). *Physician Assistant Scholarly Project Posters*. 86.  
[https://commons.und.edu/pas-grad-posters/86](https://commons.und.edu/pas-grad-posters/86)

This Poster is brought to you for free and open access by the Department of Physician Studies at UND Scholarly Commons. It has been accepted for inclusion in Physician Assistant Scholarly Project Posters by an authorized administrator of UND Scholarly Commons. For more information, please contact zeinebyousif@library.und.edu.
Abstract
There is a strong established relationship between diabetes and cardiovascular disease. Much of the latest research studies have identified a link between the inflammatory processes and the pathogenesis of both type 2 diabetes and cardiovascular disease. Specific inflammatory markers include: Interleukins 1, 6, 8, C reactive protein, Fibrinogen, Tumor Necrosis Factor-α, PAI-1 and cell adhesion molecules. As a result, there has been an emphasis on identifying therapeutic approaches that would improve both markers of inflammation and glucose control. The endocrine hormones known as incretins, glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), are produced in the gastrointestinal tract following ingestion of a meal. In individuals with type 2 diabetes, endothelial dysfunction associated with premature atherosclerosis has been well documented. The purpose of this paper is to determine whether increasing levels of GLP-1 reduces markers of inflammation while improving both glucose control and cardiovascular risk factors. The review of literature explored the impact of increasing GLP-1, either through DPP-4 inhibitors or GLP-1 agonists on various inflammatory markers in patients with type 2 diabetes. The studies reviewed provided ample support for the use of DPP-4 inhibitors to improve both glycemic control and cardiovascular risk factors. GLP-1 agonists also appear to have a similar impact, but with the added benefit of weight loss. In addition, patients with type 2 diabetes frequently have coagulation abnormalities leading to a prothrombotic state. Thus the reduction in fibrinogen, C-reactive protein and plasminogen activator inhibitor observed during the review of literature supports the potential for DPP-4 inhibitors and GLP-1 agonists to exhibit anti-thrombotic effects. These findings are of clinical significance as these treatments may potentially slow the progression of premature cardiovascular disease as well as reduce thrombotic events in patients with type 2 diabetes.

Introduction
The relationship between diabetes and cardiovascular disease has been the focus of many empirical investigations. Across time, researchers have explored a link between inflammatory processes and the pathogenesis of both diabetes and cardiovascular disease. Consequently, there has been an emphasis on identifying therapeutic approaches that would improve both markers of inflammation and glucose control, thereby slowing the progression of premature cardiovascular disease in patients with type 2 diabetes. The purpose of this review is to examine the role of increased levels of GLP-1 in reducing markers of inflammation.

Statement of the Problem
Given the known relationship between diabetes, premature cardiovascular disease and the inflammatory involvement, it is important to explore inflammatory markers and therapies that may reduce their negative impact on endothelial function.

Research Question
In patients with type 2 diabetes, does increasing GLP reduce markers of inflammation while improving both glucose control and cardiovascular risk factors.

Literature Review
• An article search of the following electronic medical databases was conducted: PubMed, The Cochrane Library, DynaMed and MEDLINE. A combination of keywords and subject headings were used in search terms including: type 2 diabetes, DPP-4 inhibitors, GLP-1 inhibitors, agonist, incretins, cardiovascular disease.
• Full articles were retrieved for further review if the information given suggested that the study: included patients with type 2 diabetes mellitus, measured pre and post markers of inflammation, cardiovascular risk factors or changes in glucose following either a DPP-IV inhibitor or a GLP-1 agonist active intervention.
• Pettigrew, et al. assessed the effect of Liraglutide GLP-1 on markers of inflammation and glucose control in patients with type 2 diabetes. The author expresses sincere appreciation to both Terri Pettigrew K. A. M. (2008). Beneficial effects of once daily GLP-1 analogues, as seen with DPP-4 inhibitors, is the reduction in the inflammatory markers independent of changes in weight. Oxidative stress as measured by FPG was found to also decrease with the addition of a GLP-1 analogue.

Discussion
• Based on the studies discussed, DPP-IV inhibitors have been shown to improve glycemic control and, based on the small trials, appear to have great potential to provide beneficial cardiovascular effects due to their positive impact on reducing inflammatory markers.
• GLP-1 agonists also appear to have similar benefits as DPP-IV inhibitors with the added benefit of weight loss. In addition, patients with type 2 diabetes frequently have coagulation abnormalities leading to a prothrombotic state. Thus the reduction in fibrinogen, C-reactive protein and plasminogen activator inhibitor observed during the review of literature supports the potential of DPP-IV inhibitors and GLP-1 agonists having an anti-thrombotic effect.
• A decrease in HgbA1c, inflammatory markers (e.g. CRP, TNF-α), Free Fatty Acids and Triglycerides were common themes presented during the review of literature looking specifically at the role of DPP-IV inhibitors and their impact on increasing GLP-1.
• DPP-IV inhibitors have been shown to be well tolerated, weight neutral and less expensive. They do, however have less of an impact on A1c as compared to the GLP-1 analogues.
• A common theme found with GLP-1 analogues, as seen with DPP-IV inhibitors, is the reduction in the inflammatory markers independent of changes in weight. Oxidative stress as measured by FPG was found to also decrease with the addition of a GLP-1 analogue.
• Hypoglycemic events were essentially non-existent with DPP-IV inhibitors and GLP-1 analogues.

Applicability to Clinical Practice
• The findings of this research project are applicable to several areas of clinical practice. The literature supports the anti-inflammatory effect of both DPP-IV inhibitors and GLP-1. While these pharmacologic therapies have been on the market for over a decade, there utilization is not optimized.
• Given the minimal risk of hypoglycemia associated side effects with both DPP-IV inhibitors and GLP-1 analogs, as well as their impact on HgbA1c reduction, it seems most appropriate for there to be a shift in the prescribing habits of clinicians as they work with patients to help achieve improved glycemic control.
• Both of these classes of therapy have been shown to reduce markers of inflammation, which shows promising in reducing the progression of cardiovascular disease and possibly thrombotic events.
• Clinicians will be assisting patients with not only managing glycemia with anti-diabetes medications, but also cardiovascular risk factors. Lifestyle modification, albeit challenging for patients to embrace and sustain, is part of the practice guidelines regardless of where the patient falls in the algorithm and should remain part of the treatment plan.
• Clinicians should be working with patients to enhance management of all comorbidities associated with diabetes, especially cardiovascular. It seems reasonable to select diabetes medications that will target both chronic diseases. There are oral medications, on the market that have combined DPP-IV inhibitors with metformin.
• Clinicians need to be current and relevant in both medical and pharmacologic knowledge, which impacts their prescribing habits and quality of patient care.

References

Acknowledgements
The author expresses sincere appreciation to both Terri Pettigrew and Dr. Sue Kunz who served as faculty advisors and mentors for this project. It has been a pleasure working with both of you as well as the rest of the faculty and staff within the Department of Physician Assistant Studies at the University of North Dakota School of Medicine and Health Sciences.


Impact of Increasing GLP-1 on Markers of Inflammation, Glucose Control and Cardiovascular Risk Factors in Patients With Type 2 Diabetes
Kristina Sandstedt, MS, CDE, PA-S
Department of Physician Assistant Studies, University of North Dakota School of Medicine & Health Sciences
Grand Forks, ND 58202-9037