The Effects of GLP-1 Analog Use upon C-peptide levels in Patients with Type 2 Diabetes Mellitus

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Introduction

Type 2 Diabetes Mellitus (T2DM) affects growing numbers of patients in the United States. T2DM is characterized initially by an increase in the production of insulin by the pancreas. Over time, as pancreatic beta cells fail to function, levels of circulating insulin are reduced. Alterations in insulin levels can be measured by measuring C-peptide. The purpose of this study is to describe the effects of a class of medications known as GLP-1 analogs on C-peptide levels in patients with T2DM.

Background/Review of Literature

Rates of T2DM in the United States are rising, with an estimated 18.8 million diagnosed with T2DM in 2010 and 7 million undiagnosed patients. In the state of Alabama, Diabetes Mellitus is the 6th leading cause of death. Improving methods of assessing and treating patients with diabetes is an essential component of reducing mortality and expense associated with the disease.

C-peptide is a 31 amino acid residue derived from proinsulin, and was first described in 1967. As insulin is released from pancreatic beta cells, C-peptide is cleaved from insulin, because C-peptide is not extracted from the liver as insulin is, it is viewed as a more direct reflection of endogenous insulin secretion.1 Though initially considered to be biologically inert, recent research suggests that alterations in C-peptide levels may play a role in the development of diabetic neuropathy and nephropathy in patients with Type 1 Diabetes Mellitus (T1DM).2 Patients with T2DM who have even minimal sustained secretions of C-peptide have a significant reduction in risk of microvascular complications compared to those patients in which C-peptide secretion is absent.3 This may be due to the proposed anti-inflammatory effects of C-peptide upon the vascular endothelium and vascular smooth muscle cells.4

Elevated levels of C-peptide are an indicator of hypersecretion of insulin, caused by the insulin resistance that is characteristic of T2DM. Patients with T2DM who have supranormal C-peptide levels have been associated with the presence of atherosclerotic plaques, possibly because of its role in regulating endothelial cell function and microvascular blood flow.4 Elevated basal C-peptide levels in T2DM patients have been associated with increased carotid intimal medial thickness, and so may be viewed as a surrogate marker for the presence of subclinical atherosclerosis in these patients.5,6

A recent development in the field of diabetes care has been the introduction of GLP-1 analogs, a category of drugs that are designed to improve glycemic control while reducing the risk of hypoglycemia. In patients with T2DM, the authors’ clinical practice, changes in C-peptide levels have been noted after the addition of GLP-1 analogs to the pharmacoeconomic regimen of patients with T2DM. Though multiple studies on the effects of GLP-1 analogs to weight, glycemic control, and cardiovascular risk in patients with T2DM can be found in the literature, little is known about the effects of the analogs upon discrete clinical markers such as C-peptide and serum creatinine. There is a growing body of evidence that underscores the importance of preserving endogenous insulin secretion7, which is supported by clinical experiences of the authors.

Purpose of the Study

The purpose of this study is to describe the effects of GLP-1 analogs upon the C-peptide levels of patients with T2DM.

Methods

After approval by the Institutional Review Board of the University of Alabama in Huntsville, a chart abstraction began. More than 500 closed charts from a medical practice specializing in endocrinology were conducted. Inclusion criteria were:

- Age of 19 years or older
- Previous diagnosis of T2DM
- Use of GLP-1 analog therapy (exenatide or lixisenatide)
- C-peptide measurement before initiation of GLP-1 analog therapy and minimum of once while using the medication

Sample Characteristics

The sample is composed of 174 patients who met the criteria. The average age of the sample population was 56.1 years. The average number of years since diagnosis of T2DM was 13.07 years.

Results

Table 1-HBA1c changes derived from sample.

Table 2. Patient self-reports of hypoglycemic episodes associated with addition of lixisenatide or exenatide to existing medication regimens.

Discussion

Though relationships between C-peptide, HBA1c, and serum creatinine overall lacked statistical significance in this study, the results do seem to suggest that when GLP-1 analogs are added to existing classes of antidiabetic therapy (biguanides, thiazolidinediones, metformin, and sulfonylureas), there is a reduction in HBA1c, which would be beneficial in determining the significance of GLP-1 analog use upon clinical markers of complications in this patients affected by T2DM. In addition, research upon the identification and description of the receptor for proinsulin C-peptide, including the possible differences in receptor sites and action for patients with both T1DM and T2DM is also warranted.

Conclusions and Future Research

This study reports real-world effects of GLP-1 analog use in patients with T2DM upon clinical markers linked to microvascular and macrovascular complications. Outcomes and effectiveness reported involving larger groups of patients in more sustained treatment periods could be beneficial in determining the significance of GLP-1 analog use upon clinical markers of complications in this patients affected by T2DM. In addition, research upon the identification and description of the receptor for proinsulin C-peptide, including the possible differences in receptor sites and action for patients with both T1DM and T2DM is also warranted.