Demographic and Clinical Characteristics of Patients With Type 2 Diabetes Mellitus Initiating Dipeptidyl Peptidase 4 Inhibitors: A Retrospective Study of UK General Practice

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ABSTRACT

Purpose: The majority of people with type 2 diabetes mellitus (T2DM) will develop chronic kidney disease in their lifetime. Because most dipeptidyl peptidase (DPP)-4 inhibitors require dose adjustment in patients with T2DM and renal impairment, we aimed to understand how these treatments are prescribed in UK clinical practice, and to determine whether recommended dose adjustments are being made at initial prescription.

Methods: This retrospective, descriptive cohort study analyzed data from the Clinical Practice Research Datalink (CPRD). Patients of interest were those with T2DM and renal impairment initiated on a DPP-4 inhibitor between 2014 and 2015. Patients under 40 years of age and with type 1 diabetes were excluded. Descriptive statistics were calculated for baseline demographic and clinical characteristics, and the study protocol was approved by the Independent Scientific Advisory Committee for Medicines and Healthcare products Regulatory Agency database research.

Findings: A total of 3425 patients diagnosed with T2DM and renal impairment and initiated on a DPP-4 inhibitor were identified. The percentages of patients prescribed the high dose of saxagliptin, alogliptin, sitagliptin, and vildagliptin were 48%, 43%, 41%, and 27%, respectively, which is not recommended given their renal dysfunction. These are conservative estimates, as they do not include patients with severe renal impairment on sitagliptin and alogliptin, whose doses should be further reduced. No patients were prescribed an inappropriately high dose of linagliptin, as there is no requirement for dose adjustment in patients with renal impairment.

Implications: In this study, a considerable number of patients with T2DM and renal impairment were prescribed an inappropriately high dose of saxagliptin, alogliptin, sitagliptin, or vildagliptin for their level of renal impairment at treatment initiation. This prescribing could have been due to the complexity of different dosing requirements, or a lack of awareness of the need for dose adjustment of most DPP-4 inhibitors in patients with renal impairment. Linagliptin may be used in patients with moderate or severe renal impairment without dose adjustment. (*Clin Ther*. 2016;38:1825–1832) © 2016 The Authors. Published by Elsevier HS Journals, Inc.

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INTRODUCTION

The association between type 2 diabetes mellitus (T2DM) and renal impairment is well-established,

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with several studies reporting the increased risk for renal failure in patients with T2DM.[1–4] UK-based studies suggest that people with T2DM have a 4.5- to 6-fold increased risk for developing moderate to severe chronic kidney disease.[5] Diabetes is also the leading cause of end-stage renal disease in the United Kingdom,[6] and ~30% of people with T2DM have clinically significant renal impairment.[4,6]

A number of commonly used antidiabetic medications are not recommended in individuals with moderate[7] or severe[8,9] renal impairment (estimated glomerular filtration rate [eGFR] <60 mL/min/1.73 m^2). For example, metformin and the sulfonylureas, which are recommended as first-line treatments by the National Institute for Health and Care Excellence, should be used with caution in patients with renal impairment.[10] Newer classes of antidiabetic medicines have now been licensed for the treatment of T2DM, including dipeptidyl peptidase (DPP)-4 inhibitors. These agents give clinicians and patients more options in the management of T2DM. Five drugs are available within the DPP-4 inhibitor class: alogliptin, linagliptin, saxagliptin, sitagliptin, and vildagliptin.

While DPP-4 inhibitors offer more flexibility for patients with renal impairment, each member of the class requires a different level of dose adjustment depending on kidney function (Table I [11–15]). Sitagliptin,[11] saxagliptin,[14] vildagliptin,[13] and alogliptin[12] require different dosing strategies if patients have moderate to severe renal impairment. Linagliptin does not require dose adjustment in these patients, as it is excreted via the bile and feces, with <5% excreted via the kidneys.[15] The different requirements mean that there is a risk that some patients with T2DM and renal impairment may not be prescribed a recommended dose according to their level of renal impairment. There is thus a need to review the doses of DPP-4 inhibitors prescribed to these patients, in comparison with the recommendations in the summary of product characteristics (SPC) of each medicine.

In addition, the National Institute for Health and Care Excellence recently updated its clinical guideline on T2DM.[10] As such, it would also be useful to describe the characteristics of patients with T2DM treated with DPP-4 inhibitors, as well as how these characteristics are used in the treatment pathway, to compare clinical practice with the new guidelines.

The observational data available in the Clinical Practice Research Datalink (CPRD) are representative of routine primary care in the United Kingdom, and therefore provide a way of gaining insight into both patient characteristics and adherence to guidelines in the treatment of T2DM in the United Kingdom.[16]

MATERIALS AND METHODS

Study Design

This retrospective, descriptive cohort study analyzed data from patients with T2DM and renal impairment who were initially prescribed a DPP-4 inhibitor. The drug and dosage prescribed, as well as the appropriateness of this prescription based on each patient's level of renal impairment, were then evaluated based on the first DPP-4 inhibitor prescribed.

Table I. Thresholds for dose adjustment.

	Level of Renal Impairment		
Drug	CrCl ≥50 mL/min	CrCl 30–<50 mL/min	CrCl <30 mL/min (Including ESRD*)
Sitagliptin[11]	100 mg	50 mg	25 mg
Alogliptin[12]	25 mg	12.5 mg	6.25 mg
Vildagliptin[13]	50 mg BID	50 mg once daily	
Saxagliptin[14]	5 mg	2.5 mg	
Linagliptin[15]	All Levels of Renal Impairment 5 mg		

CrCl = creatinine clearance; ESRD = end-stage renal disease.
*Except saxagliptin, which is not recommended for use in patients with end-stage renal disease requiring hemodialysis.