Sulfonylurea Prescribing Patterns After the Introduction of DPP-4 Inhibitors and GLP-1 Receptor Agonists

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ABSTRACT

Purpose: Although newer agents (dipeptidyl peptidase [DPP]-4 inhibitors and glucagon-like peptide [GLP]-1 receptor agonists) are available for the treatment of hyperglycemia in patients with type 2 diabetes mellitus (T2DM), the impact of the availability of these agents on the use of second-generation sulfonylureas (SUs) is unknown. This article presents percentages of patients prescribed SUs, using data from the National Ambulatory Medical Care Survey (NAMCS). The associations between SU prescribing and prespecified variables of interest were also explored.

Methods: The NAMCS database was queried for visits of patients aged ≥18 years with an International Classification of Diseases, Ninth Revision diagnostic code relevant to T2DM. χ^2 tests were conducted to assess the associations between SU use and year-group (2003–2004, 2007–2008, or 2009–2010) and other variables of interest. A multivariate logistic regression model was constructed to jointly assess the value of these variables in predicting SU use. All analyses were weighted using procedures recommended by the National Center for Health Statistics.

Findings: Data from 7042 eligible visits were included, representing an extrapolated national estimate of 280,733,405 patient visits. The percentages of patients who received a prescription for an SU, by study year, were 25.7%, 23.4%, and 23.7% in 2003 to 2004, 2007 to 2008, and 2009 to 2010, respectively ($P = 0.57$). In the multivariate model, age ≥70 years, male sex, nonwhite race, primary care physician seen, and concurrent DPP-4 inhibitor use were significantly associated with SU use.

Implications: No significant decrease in the use of SUs was observed after the introduction of DPP-4 inhibitors and GLP-1 receptor agonists. However, patient-specific factors (eg, select demographic variables, site of care, and concurrent medication use) were associated with SU use. (*Clin Ther*. 2015;37:1477–1482)

Key words: diabetes, endocrinology, prescribing patterns, standards of practice, sulfonylureas, type 2.

INTRODUCTION

The Centers for Disease Control and Prevention recently estimated that 9.3% of the US population (or 29.1 million people) have diabetes.[1] In adults ≥20 years of age, this estimation increases to 12.3%.[1,2] The cost of this disease in 2012 was approximately (US) $245 billion.[3] In contrast to the rising prevalence of confirmed diabetes, the prevalence of undiagnosed cases has declined, suggestive of improvements in screening and diagnosis.[4] As the number of patients living with diabetes continues to increase, health care providers are faced with the task of treating more and more patients at varying stages of the disease.[5] A patient's unique social or medical factors, as well as a patient's and/or provider's preferences, may influence drug-therapy selection and treatment outcomes.

Metformin has a longstanding reputation as the drug of choice for the initial treatment of type 2 diabetes mellitus (T2DM).[6,7] Most treatment algorithms and guidelines promote metformin as the drug of choice due to its safety and efficacy profiles.[6–8]

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However, when further reduction in glycemic control is needed, or when metformin is not appropriate, controversy exists as to the order in which to add second-line agents.[6,8] Second-generation sulfonylureas (SUs) (eg, glipizide, glyburide, glimepiride) may be used either as monotherapy or as an adjunct to metformin. Advantages of SUs include extensive clinical experience and low cost. Most of the agents in this class have been on the market for 2 decades, with generic formulations available. Disadvantages include increased risks for hypoglycemia and weight gain.[6–8]

The introduction of the dipeptidyl peptidase (DPP)-4 inhibitor class (eg, sitagliptin, saxagliptin, linagliptin, alogliptin) in 2005 provided oral treatment options that are associated with weight neutrality and low rates of hypoglycemia.[6] Another newer class of medication, glucagon-like peptide (GLP)-1 receptor agonists (eg, exenatide, liraglutide, albiglutide), was introduced in 2006. Although these agents provide a low risk for hypoglycemia and may induce weight loss, they can be expensive (relative to SUs), and they are available only in subcutaneously injectable formulations.[6–8]

Despite the high cost of these new therapies, it was anticipated that the use of SUs would decrease after the introduction of the DPP-4 inhibitors and GLP-1 receptor agonists.[7] A study that examined trends in the patterns and costs of drug treatment of T2DM reported that between 2008 and 2013, drug expenditures for diabetes increased by 61%, driven primarily by long-acting insulin, DPP-4 inhibitors, and GLP-1 receptor agonists.[9] Although some research has reported that SU use has decreased over time, the impact of the availability of these new agents on the use of SUs is unknown.[9]

The purpose of this study was to determine the impact of the availability of DPP-4 inhibitors and GLP-1 receptor agonists on the prescribing patterns of SUs. In addition, we explored the influence of select patient-related factors on the prescribing patterns of SUs.

PATIENTS AND METHODS

The primary objective of this study was to compare percentages of patients prescribed SUs versus DPP-4 inhibitors and GLP-1 agonists, using data from the National Ambulatory Medical Care Survey (NAMCS) recorded in 2003 to 2004, 2007 to 2008, and 2009 to 2010. The secondary objective was to explore the association between prespecified variables and the use of SUs. The NAMCS is an annual, national probability sample of visits made to the offices of non–federally employed physicians classified by the American Medical Association or the American Osteopathic Association as "office-based, patient care."[10] Further details regarding the NAMCS can be found in the **Appendix** in the online version at 10.1016/j.clinthera.2015.04.011.

NAMCS datasets covering 6 years (2003–2004 and 2007–2010) were included in this study. Data from survey visits of patients 18 years of age or older with an International Classification of Diseases, Ninth Revision, diagnostic code relevant to T2DM in the primary, secondary, or tertiary diagnostic field (250.00, 250.02, 250.10, 250.12, 250.20, 250.22, 250.30, 250.32, 250.40, 250.42, 250.50, 250.52, 250.60, 250.62, 250.70, 250.72, 250.80, 250.82, 250.90, 250.92) were included in the dataset. This study contained no explicit exclusion criteria. Target medication use was detected according to visit year. Since 2006, drug characteristics in the NAMCS have been assigned with Multum's Lexicon Drug Database (http://www.multum.com). Therapeutic classification reflects Multum's 3-level nested-category system. In previous years, the US Food and Drug Administration's National Drug Code directory had been used for therapeutics classification (http://www.accessdata.fda.gov/scripts/cder/ndc/default.cfm).

All analyses were weighted using the appropriate SURVEY procedures in SAS version 9.3 (SAS Institute Inc, Cary, North Carolina), as recommended by the National Center for Health Statistics (NCHS).[11] The survey data were analyzed using the sampled visit weight that is the product of the corresponding sampling fractions at each stage in the sample design. The sampling weights have been adjusted by NCHS for survey nonresponse as appropriate within each database, yielding an unbiased national estimate of visit occurrences, percentages, and characteristics.

Because of the complex sample design, sampling errors were determined using the SAS SURVEYFREQ and SURVEYLOGISTIC procedures, which take into account the clustered nature of the sample.[6] The appropriate NOMCAR and DOMAIN statements/options were implemented in these procedures, as recommended by the NCHS. The dependent variable of interest was SU use (yes vs no), in which the denominator was the number of cases meeting the inclusion/exclusion criteria. SU use was defined using the appropriate medication codes found in any of the MED1-8 or DRUGID1-8 medication fields.[7]