Progression to Insulin for Patients with Diabetes Mellitus Using the Texas Medicaid Database

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ABSTRACT

Background: Patients newly diagnosed with type 2 diabetes mellitus generally initiate therapy with either metformin [Met] or a sulfonylurea [SU] drug, followed by the addition of a second agent (Met, an SU drug, or a thiazolidinedione [TZD] drug) if the diabetes is not well controlled. If necessary, the usual third line of treatment is the addition of insulin.

Objective: The purpose of our study was to compare the progression to insulin among 3 cohorts receiving the oral antidiabetic (OAD) drug combinations Met/SU, Met/TZD, or SU/TZD.

Methods: This study used data from the Texas Medicaid database. The date of addition of a second OAD was considered a patient's index date and patients were followed for up to 5 years. Cox proportional hazards regression compared the progression to first insulin use among cohorts, using the Met/SU cohort as the reference group, while adjusting for demographics, comorbidities, and propensity scores.

Results: A total of 4083 patients were included in the study (Met/SU = 2872, Met/TZD = 438, and SU/TZD = 773). Insulin was added to the medication regimen of patients by the end of follow-up in 19.7% of the Met/SU cohort, 17.6% of the Met/TZD cohort, and 26.3% of the SU/TZD cohort. The adjusted Cox proportional model estimated that patients in the SU/TZD cohort had a 40% higher probability of progression to insulin than patients in the Met/SU cohort (odds ratio [OR] = 1.40; 95% CI, 1.19–1.64), whereas there was no significant difference between the Met/TZD and Met/SU cohorts (OR = 0.85; 95% CI, 0.67–1.08).

Conclusions: It appears that mechanism of action may play a role in progression to insulin for concomitant OAD agents. A slower progression to insulin was seen for patients receiving a paired sensitizer regimen (ie, Met/TZD) compared with those receiving a secretagogue sensitizer regimen (ie, SU/TZD). (*Clin Ther.* 2011;33: 2016–2020)

Key words: diabetes, insulin, oral antidiabetics, metformin, sulfonylurea.

INTRODUCTION

Type 2 diabetes mellitus is marked by a progressive deterioration in the body's ability to control glucose concentrations.[1] After diagnosis, diet and exercise regimens are implemented in addition to the initiation of a single oral antidiabetic (OAD) agent such as a sulfonylurea (SU) drug or metformin (Met) (standard therapy). When monotherapy is no longer effective, combination oral therapy may be prescribed. Common combinations are Met plus an SU drug, Met plus a thiazolidinedione (TZD) drug, or an SU drug plus a TZD drug. Previous studies have shown that adding a TZD drug to standard oral therapy has resulted in superior clinical outcomes over a Met/SU regimen.[2–5]

If glycemic control cannot be achieved despite combination therapy of OAD medications, insulin may be prescribed. Research indicates that after 3 to 5 years of follow-up, 20% to 25% of patients receiving OAD medications are prescribed insulin (ie, about 5% per year).[6–10] Of the 27 million patients with diabetes, about 4 million (15%) are covered by Medicaid. These beneficiaries account for a substantial portion of Medicaid program costs (16%), even though they are a relatively small percentage of the Medicaid population (6%).[11]

The objective of our study was to conduct a retrospective analysis of the Texas Medicaid database to compare (1) the percentage of patients who began insulin therapy and (2) progression to insulin—a combination of the percent of patients who began insulin therapy and the time to first insulin prescription—for those who had insulin

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added to their medication regimen (a possible indicator of poor diabetes control) among different OAD medication combinations, controlling for baseline demographic and comorbidity measures.

The primary objective was to compare 3 cohorts of patients—those receiving index combination of (1) Met/SU, (2) SU/TZD, or (3) Met/TZD.

METHODS

Paid prescription drug claims and demographic data (age and gender) were extracted from the Texas Medicaid Vendor Drug Program's prescription claims database for all patients receiving an SU drug or Met from January 1, 2000 to December 31, 2007.

Patients were included in the study if they were receiving monotherapy with either an SU drug or Met for at least 1 year before having a second OAD medication added to their regimen. Female patients who had a prescription for prenatal vitamins during the study period were excluded because it was possible that they had gestational diabetes. The day a second type of OAD medication was added (or the day a patient was switched to a fixed-dose combination OAD medication) was considered to be that patient's index date. Three cohorts were formed as described earlier (ie, Met/SU, SU/TZD, and Met/TZD). These cohorts were followed for up to 5 years to determine progression to insulin use. First the percentage of patients who advanced to insulin during the follow-up period was calculated. Insulin use was defined as ≥2 outpatient prescriptions for insulin. To incorporate both the time to insulin and whether insulin was added during the follow-up period, survival curves for the 3 cohorts were used to compare differences in progression to insulin. Cox proportional hazards regression analysis comparing the primary outcome (ie, progression to insulin) among the 3 cohorts was conducted, using the Met/SU cohort as the comparator group, while adjusting for demographics (gender and age), comorbidities, and propensity scores. The Met/SU cohort was used as the comparator group because it contained the largest number of patients of the 3 cohorts. Von Korff's Chronic Disease Score (CDS) was used to estimate comorbidity weights because each patient's score can be calculated by analyzing patterns of other selected prescription medications.[12] Propensity scores indicate the probability that a patient is prescribed a particular treatment given a set of known covariates. The propensity to be treated with a Met/SU combination was calculated based on baseline covariates and these scores were collapsed into quintiles, with a higher quintile indicating a higher propensity. Statistical analyses were conducted using SAS 9.2 (SAS Institute Inc, Cary, NC), and an a priori level of significance of 0.05 was used. This study was approved by the Institutional Review Board of the University of Texas at Austin.

RESULTS

Patient Baseline Data

A total of 4083 patients receiving Medicaid benefits met the study criteria: 2872 in the Met/SU cohort, 438 in the Met/TZD cohort, and 773 in the SU/TZD cohort (Table I). For the Met/SU cohort, mean age was 65 (14) years, 69% were female, and mean CDS was 5.9 (2.6). For the Met/TZD cohort, mean age was 61 (15) years, 75% were female, and mean CDS was 6.1 (2.6). For the SU/TZD cohort, mean age was 69 (13) years, 70% were female, and mean CDS was 6.2 (2.7). By the end of the follow-up period, the percentage of patients who had insulin added to their regimen was 19.7% in the Met/SU

Table I. Baseline patient information by medication combinations. Data given as mean (SD) unless otherwise specified.

Characteristic	Met/SU (n = 2872)	Met/TZD (n = 438)	SU/TZD (n = 773)	Total (N = 4083)
Age, y	64.6 (13.8)	61.3 (14.7)	68.7 (12.9)	65.0 (13.9)
Gender, % female	68.7	74.9	70.0	69.6
Chronic disease score	5.92 (2.61)	6.07 (2.59)	6.22 (2.72)	6.00 (2.64)
Receiving insulin by end of follow-up, no. (%)	565 (19.7)	77 (17.6)	203 (26.3)	845 (20.7)

SU = sulfonylurea; TZD = thiazolidinedione.