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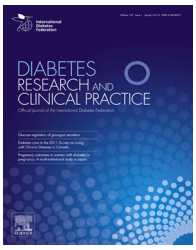

Evaluation of the relationship between weight change and glycemic control after initiation of antidiabetic therapy in patients with type 2 diabetes using electronic medical record data

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ABSTRACT

Aims: This study evaluates the relationship between HbA1c and weight change outcomes by anti-diabetic weight-effect properties in patients newly treated for type 2 diabetes; a relationship not previously characterized.

Methods: Electronic medical records of patients with type 2 diabetes newly prescribed anti-diabetic monotherapy were assessed to identify HbA1c goal attainment [(<53 mmol/mol)] and weight change at 1-year. Anti-diabetics were categorized by weight-effect properties: weight-gain (sulfonylureas, thiazolidinediones) and weight-loss/neutral (metformin, DPP-4 inhibitors, GLP-1 agonists). Logistic regression analyses identified likelihood of attaining HbA1c goal or ≥3% weight loss by anti-diabetic category controlling for baseline characteristics. MANOVA was used to identify correlation between changes in weight and HbA1c.

Results: The study included 28,290 patients. Mean age ± sd was 61 years ± 11.8. Baseline HbA1c was 7.4% ± 1.6 (57 mmol/mol ± 17); 67.3% were prescribed a weight-loss/neutral anti-diabetic. At 1-year, more patients in the weight-loss/neutral anti-diabetic category lost weight (≥3%) than in the weight-gain anti-diabetic category (40.4% vs. 24.2%, $p < 0.001$) or had an HbA1c < 7.0% (<53 mmol/mol) (71.1% vs. 63.8%, $p < 0.001$). Those prescribed a weight-gain anti-diabetic were 53% less likely to lose weight and 29% less likely to be at HbA1c goal than those prescribed a weight-loss/neutral anti-diabetic ($p < 0.001$). Weight loss and HbA1c outcomes were significantly correlated ($p < 0.001$).

Conclusions: Weight loss of ≥3% was associated with better glycemic control in patients newly treated for type 2 diabetes. Anti-diabetics associated with weight-loss/neutrality were associated with greater weight loss and HbA1c goal attainment and may facilitate efforts to co-manage weight and glycemia in the ambulatory-care setting.

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1. Introduction

Weight management, in addition to glycemic control, is a core component of type 2 diabetes management [1,2]. While weight reduction improves insulin resistance and glycemic control [3,4], reducing weight by as little as 1 kg also lowers the risk of type 2 diabetes progression and CV disease [5]. Despite the benefits, weight loss is challenging in the type 2 diabetes population. One study found that patients consider adhering to a moderate diet, thus being able to reduce weight, to be as much of a burden as taking insulin [6].

Complicating weight management efforts are the weight effects of anti-diabetic agents. While several newer classes of drugs are considered weight neutral (e.g., DPP-4 inhibitors) or are associated with weight loss (i.e., GLP-1 agonists), other classes of anti-diabetics are associated with weight gain (e.g., insulin, sulfonylureas and thiazolidinediones) [1,7]. Therefore, clinicians and patients must consider the glycemic control and weight effect benefits and trade-offs when planning a therapeutic course of action. Under ideal circumstances, such decisions are evidence based, and a number of studies have provided evidence associating the benefits of weight loss in patients with diabetes including improved glycemic control. While, the benefits of weight loss in improving cardiovascular events have not been clearly established [8–10], there is ample evidence that intensive glycemic control is associated with a reduction in microvascular risk [11–14]. Thus, the benefits of weight loss in diabetes in facilitating improvements in glycemic control should translate into improvement in clinical outcomes.

There is surprisingly little real-world data, however, that indicate whether treatment-emergent weight change and glycemic control go hand in hand or whether these treatment effects are independent. Specifically, numerous clinical trials and retrospective studies have looked at the impact of anti-diabetic medications on weight change and glycemic control as independent outcomes. In addition, a small number of studies have evaluated the impact of weight change on HbA1c levels, but these studies have given little consideration to drug therapy and their weight-effect properties [15–17]. To our knowledge, no studies have further assessed the influence of anti-diabetic medications on weight and HbA1c outcomes simultaneously, while considering the weight-effect properties of the medications. Our objective was, therefore to begin to close this evidence gap by evaluating the association between weight change and glycemic control in patients with type 2 diabetes, considering the weight-modifying properties of prescribed anti-diabetic therapy.

2. Material and methods

2.1. Study design, timeline, and data

This retrospective cohort study evaluated weight and HbA1c outcomes in patients with type 2 diabetes newly treated with anti-diabetic monotherapy in routine clinical practice.

Patients were identified in the General Electric (GE) Centricity EMR research database from January 1, 2000 through June 30, 2010. The GE EMR contains ambulatory electronic health records for over 15 million patients treated by 15,000 physicians, two-thirds of which practice in a primary care setting. The database contains longitudinal patient data including demographic information (e.g., age, gender, race and location); clinical data (e.g., vital signs, laboratory test orders and results); and medication list entries and prescription orders. The GE EMR population represents 42 of 50 US states, is older than the US population, and predominantly has commercial insurance [18]. Approximately 7.0% of patients in the EMR have a diagnosis for diabetes [19] versus 8.3% of the US population [20].

2.2. Study population

Patients with type 2 diabetes were identified based on documentation of one or more of the following: an International Classification of Diseases, Ninth Revision (ICD-9) diabetes diagnosis code of 250.×0 or 250.×2; two consecutive fasting blood glucose levels $\geq$ 126 mg/dL; a random blood glucose $\geq$ 200 mg/dL; an HbA1c level $\geq$ 7.0% ($\geq$53 mmol/mol); or treatment with any anti-diabetic drug. Patients with diagnoses for type 1 diabetes (ICD-9 codes 250.×1 or 250.×3) were excluded.

Study patients were required to be 18+ years of age, with a new, first-line prescription order for metformin (MET), sulfonylurea (SU), thiazolidinedione (TZD), DPP-4 inhibitor, or GLP-1 analog with no documented anti-diabetic therapy for at least 395 days prior to the index date. A 395-day wash-out period was employed because prescription orders for chronic medications may only appear in the EMR at the time of annual renewal. An additional month beyond the prescription year allowed for a lag between the prescription expiration and a new prescription order. Patients initiated on a class of anti-diabetic not listed above, including insulin, were not included as these agents are not commonly used as first-line therapy.

Patients receiving prior therapy or multiple anti-diabetic agents on index date were excluded to avoid confounding or challenges in categorizing patients on combination of drugs with different effects on weight. If patients were prescribed a different class of anti-diabetic within 30 days after index date, this prescription was considered a switch in therapy and the second prescribed class was assigned as the index date drug. Changes after 30-days post-index were considered add-on therapy and did not affect index-date drug assignment. Eligible patients were active in the EMR for 410 days prior to and after the index date that represents 1 year plus an additional 45-day window to capture relevant clinical data.

2.3. Study outcomes

Study outcomes were change in weight and change in HbA1c from baseline to 1 year (±45 days) after the initiation of anti-diabetic therapy. Follow-up HbA1c was categorized as at goal if HbA1c <7.0% (<53 mmol/mol) or not at goal if HbA1c $\geq$ 7.0% ($\geq$53 mmol/mol). Weight was categorized as weight gain (increase of $\geq$3%), weight loss (decrease of $\geq$3%), or weight neutral (weight change <3%). A change in body weight of 3% is considered to be clinically meaningful and not likely due to measurement error or normal weight fluctuation [21,22].