Contents lists available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

Direct costs associated with initiating NPH insulin versus glargine in patients with type 2 diabetes: A retrospective database analysis

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ARTICLE INFO

Article history:
Received 12 November 2008
Received in revised form
27 August 2009
Accepted 28 September 2009
Published on line 5 November 2009

Keywords:
Glargine
Neutral protamine hagedorn
Hypoglycemia
Diabetes
Cost
Propensity score matching

ABSTRACT

Aims: To compare total costs and risk of hypoglycemia in patients with type 2 diabetes (T2D) initiated on NPH insulin versus glargine in a real-world setting.
Methods: This study used claims data (10/2001 to 06/2005) from a privately insured U.S. population of adult T2D patients who were initiated on NPH or glargine following a 6-month insulin-free period. A sample of 1698 glargine-treated and 400 NPH-treated patients met the inclusion criteria. Total and diabetes-related costs (inflation-adjusted to 2006) were calculated for 6-month pre- and post-index periods and compared between 400 patient pairs matched by a propensity score method.
Results: In the post-index 6-month period, glargine patients incurred higher diabetes-related drug costs than NPH patients ($785 versus $632, $p < 0.0001$) but there were no significant differences in diabetes-related medical or total costs, or all other total cost categories. Compared to the pre-index period, glargine patient costs declined by $2420 ($p = 0.058$) whereas NPH patient costs declined by $4200 ($p = 0.046$), with no statistically significant group differences ($p = 0.469$). Among patients with hypoglycemia-related claims (0.75% in both groups), mean hypoglycemia-related costs were $85 and $202 for NPH and glargine patients, respectively ($p = 0.564$).
Conclusion: Initiation of either NPH or glargine was associated with major cost reductions and infrequent hypoglycemia-related claims.

1. Introduction

Prevalence of diabetes continues to rise in the U.S. and around the world. According to data published in 2006, the prevalence of diabetes (diagnosed and undiagnosed) among U.S. adults aged ≥20 years rose from 8.2% in 1988–1994 to 9.3% in 1999–2002 [1]. In 2007, the rate increased to 10.7%; approximately 23.5 million Americans aged ≥20 years were estimated to have diabetes [2]. Diabetes is a costly disease both from a societal perspective and at an individual patient level. The estimated annual total costs of diabetes in the U.S. in 2007 were $174 billion; consisting of $116 billion as direct costs and $58 billion

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0168-8227/$ – see front matter
doi:10.1016/j.diabres.2009.09.023

as indirect costs due to reduced productivity [3]. The per capita costs for people with diagnosed diabetes were $11,744 per year and 57% of these costs ($6649) were attributable to diabetes [3].

Improved glycemic control is strongly linked to reducing the risk of diabetes complications in type 1 (T1D) [4] and type 2 diabetes (T2D) patients [5–8]. In patients with T2D, both oral anti-hyperglycemic agents (AHAs) and insulin have been shown to reduce the risk of diabetes complications [6–8]. However, after a few years of monotherapy, suboptimal glycemic control (fasting plasma glucose $\geq$ 7.8 mmol/L and/or HbA1c $\geq$ 7.0%) was observed in approximately 50% of T2D patients in the UKPDS study [9]. Glargine (sanofi-aventis, Bridgewater, NJ) and neutral protamine hagedorn (NPH) insulin (Eli Lilly and Company, Indianapolis, IN; Novo Nordisk Pharmaceuticals, Inc., Princeton, NJ) are two commonly initiated basal insulin therapies in patients with T2D. According to a recent meta-analysis that systematically evaluated 13 head-to-head randomized controlled trials, there was no significant difference between glargine and NPH in reducing HbA1c or fasting plasma glucose [10]. In the same meta-analysis, any, symptomatic, and nocturnal hypoglycemia were significantly greater with NPH than glargine but severe and confirmed hypoglycemia were not significantly different between the two insulin therapies [10].

To date, five retrospective database analyses have been conducted to examine the economic consequences of initiating glargine and NPH (or other insulins) in the U.S. [11–15]. Three analyses were published as manuscripts [11–13], and two were published as abstracts [14,15]. NPH was the comparator to glargine in two studies [11,14] whereas other insulin therapies including NPH were the comparator to glargine in other studies [12,13,15]. The five retrospective studies varied considerably in the methods used to identify type of diabetes and hypoglycemia-related claims. Studies by Bullano et al. [11] and Miller et al. [12] included any patient with a prescription of index drug in the analysis (regardless of type of diabetes) whereas Zhang and Menditto [13] used the following criteria to isolate diabetes patients: International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) codes 250.xx or those with at least one prescription of AHAs. For identifying hypoglycemia-related claims, Bullano et al. [11] and Miller et al. [12] used ICD-9-CM codes whereas the method of identifying hypoglycemia-related claims was not specified in the publications by Zhang and Menditto [13] or Leahy et al. [14].

The results of hypoglycemia risk and direct costs also varied across the five retrospective studies. In the studies by Bullano et al. [11] and Leahy et al. [14], glargine initiation was associated with fewer hypoglycemia-related claims than NPH. The rates reported by Bullano et al. [11] were 4.8% and 6.5% for glargine and NPH, respectively. The rates reported by Leahy et al. [14] were 1.7% and 2.9% for glargine and NPH, respectively. Contrary to these findings, in the study by Miller et al. [12], the rate of hypoglycemia-related claims was greater with glargine than other insulin therapies including NPH (8.3% versus 3.5%). Among the five retrospective studies, only one study [11] estimated the mean cost of hypoglycemic event as a primary objective. The mean cost of hypoglycemic event was estimated at $1087 (95% confidence interval [CI]: $764 – 1409) [11]. In terms of estimating direct costs, glargine initiation was associated with a mean net lowering of the diabetes-related costs by $166 (95% CI: –$290 to $622) in the U.S. Veterans Affairs database [12]. In the study by Zhang and Menditto [13], there was a reduction in costs from pre- to post-index periods that was greater for glargine than other insulin therapies including NPH ($185 versus $72); however, both pre- and post-index costs were considerably greater for glargine than its comparator (glargine: $1824 – $1639 = $185; comparator: $680 – $608 = $72) [13].

The purpose of our analysis was to conduct a retrospective database analysis to compare the economic consequences of initiating glargine versus NPH specifically in T2D patients. We observed that the aforementioned retrospective studies either did not specify how the study sample was selected or did not separate T1D versus T2D patients. Also, we observed that none of the five studies excluded patients with pregnancy or gestational diabetes. Due to increased differential binding to insulin-like growth factor-1 receptors and theoretical mitogenic risk associated with glargine [16,17], NPH is more commonly prescribed than glargine for basal insulin needs during pregnancy and delivery. Not excluding patients with pregnancy or gestational diabetes could potentially over inflate the costs associated with NPH use. After isolating T2D patients and excluding pregnancy or gestational diabetes, our primary objective was to compare the total and diabetes-related medical and pharmacy costs in the 6 months before and after initiation with NPH or glargine. Our secondary objective was to compare the rates of hypoglycemia and the related medical and pharmacy costs between the two basal insulin therapies using real-world data.

2. Subjects, materials and methods

2.1. Data

Data for this analysis were obtained from a de-identified administrative claims database of more than five million privately insured individuals who received medical services from 10/2001 through 06/2005. This claims database has been used in numerous studies in various disease areas, including diabetes [18–21]. These individuals were beneficiaries in 31 large self-insured companies in the U.S. that have nationwide operations in a broad array of industries and job classifications. For employees in 17 of the 31 companies, the claims for medicals services and drugs were linked to short- and long-term disability claims records. This subset of the sample covered approximately 750,000 individuals under the age of 65, and served as the basis for this analysis.

The database included enrollment data, medical and prescription drug claims, and employee disability claims. Enrollment data included monthly eligibility, insurance type, and beneficiaries' demographic information such as age, gender, and geographic region of residence. Medical claims (e.g., hospital inpatient, hospital outpatient, office) included ICD-9-CM codes, provider payments, dates of service, and other typical claims data elements. Prescription drug claims included National Drug Codes, dosage, days supply, prescription fill dates, and payments. Disability claims included data on work loss due to absenteeism and disability. Lab results like HbA1c values were not available in this database.