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Treatment persistence after initiating basal insulin in type 2 diabetes patients: A primary care database analysis

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ABSTRACT

Aims: To compare persistence and its predictors in type 2 diabetes patients in primary care, initiating either basal supported oral therapy (BOT) or intensified conventional therapy (ICT) with glargine, detemir, or NPH insulin.

Methods: In the BOT cohort, 1398 glargine (mean age: 68 years), 292 detemir (66 years), and 874 NPH (65 years) users from 918 practices were retrospectively analyzed (Disease Analyzer, Germany: 2008–2012). The ICT group incorporated 866 glargine (64 years), 512 detemir (60 years), and 1794 NPH (64 years) new users. Persistence was defined as proportion of patients remaining on the initial basal insulin (glargine, detemir and NPH insulin) over 2 years. Persistence was evaluated by Kaplan–Meier curves (log-rank tests) and Cox regression adjusting for age, sex, diabetes duration, antidiabetic co-therapy, comorbidities, specialist care, and private health insurance.

Results: In BOT, two-year persistence was 65%, 53%, and 59% in glargine, detemir, and NPH users, respectively ($p < 0.001$). In ICT, persistence was higher without differences between groups: 84%, 85%, 86% in glargine, detemir, and NPH, respectively ($p = 0.536$). In BOT, detemir and NPH users were more likely to discontinue basal insulin compared with glargine (detemir vs. glargine: adjusted Hazard Ratio; 95% CI: 1.56; 1.31–1.87; NPH vs. glargine: 1.22; 1.07–1.38). Heart failure (1.39; 1.16–1.67) was another predictor of non-persistence, whereas higher age (per year: 0.99; 0.98–0.99), metformin (0.61; 0.54–0.69), and sulfonylurea co-medication (0.86; 0.77–0.97) were associated with lower discontinuation.

Conclusions: In BOT, treatment persistence among type 2 diabetes patients initiating basal insulin is influenced by type of insulin, antidiabetic co-medication, and patient characteristics.

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1. Introduction

In the long run insulin will be required in most type 2 diabetic patients to maintain glycemic control due to the progressive beta cell dysfunction [1]. Current guidelines from the American Diabetes Association and the European Association for the Study of Diabetes note that the majority of patients with type 2 diabetes requiring insulin therapy can be successfully treated with basal insulins [2]. Either intermediate-acting (neutral protamine Hagedorn [NPH]) or long-acting analogs such as insulin glargine or insulin detemir may be used [2]. However, because of progressive loss of endogenous insulin secretion, some patients will require additional prandial insulin therapy with short-acting insulin [2]. A Cochrane Review of randomized clinical trials comparing insulin glargine and detemir concluded that there were no clinically relevant differences in efficacy or safety, however, to achieve the same glycemic control, insulin detemir was often injected twice-daily and higher doses were needed [3]. Compared to NPH and detemir insulin glargine in addition showed fewer hypoglycemic events [4].

Several studies suggested that a large proportion of type 2 diabetes patients have difficulties managing their antidiabetic medications including insulin [5]. This often results in low treatment persistence, which has been defined as the proportion of patients who remained on treatment for a specific time or the duration of time from initiation to discontinuation of therapy [5,6]. Few studies have examined the persistence of type 2 diabetes patients on basal insulins in a real-world setting and previous results have been somewhat controversial [7,8]. In Germany, there is a lack of real-world evidence studies on the basal insulin treatment persistence and related factors in type 2 diabetes patients in primary care.

Thus, the objectives of this study were to describe persistence of basal insulin use (glargine, detemir, NPH) in type 2 diabetes patients in primary care and to determine risk factors for poor persistence. Two patient cohorts with either basal supported oral therapy (BOT) or intensified conventional therapy (ICT) were analyzed. The study applied a retrospective approach using a nationwide primary care database in Germany.

2. Patients and methods

The Disease Analyzer database (IMS HEALTH) assembles drug prescriptions, diagnoses, and basic medical and demographic data directly obtained from the practice computer system of general practitioners and diabetologists [9]. Diagnoses (ICD-10), prescriptions (Anatomical Therapeutic Chemical (ATC) Classification System) and the validity of reported data were monitored by IMS based on a number of quality assurance criteria (e.g. completeness of documentation, linkage of diagnoses and prescriptions). Because of the retrospective analysis of anonymized data from primary care practices all over Germany no specific ethical consent was obtained.

The analyzed database period was January 2008 to December 2012, and included 918 general or specialist practices throughout Germany. Patients ≥18 years old with type 2 diabetes, who had basal insulin (glargine, GLA; detemir, DET; human insulin NPH) initiated, whichever came first (defined as index), were identified. The practice visit records were used to determine 12-month prior and 24-month post index continuous follow-up, respectively. Then, type of insulin therapy (basal supported oral therapy, BOT; intensified conventional therapy, ICT) was assessed. BOT was defined if patients received basal insulin in combination with ≥1 oral antidiabetic prescription within 183 days prior and post to index and no short acting insulin (ATC: A10C1) during these time periods. ICT was defined if patients received a basal-bolus treatment with ≥1 short acting insulin within 183 days post to index. The selection process of the patients from the database is shown in detail in Fig. 1.

Basal insulin treatment persistence was defined as the proportion of patients who remained on the basal insulin treatment over 2 years after index prescription. In addition, the duration from initiation to change of insulin therapy was determined. Thus, discontinuation of basal insulin in BOT was indicated by ≥1 of the following events: prescription of another type of basal insulin, additional short acting insulin, or premixed insulin. In ICT, discontinuation was defined as use of another basal insulin or switch to premixed insulin formulations.

Potential predictors of persistence considered in the present analysis were age, sex, diabetes duration, baseline comorbidity, co-medication with oral antidiabetic drugs, diabetologist care, private health insurance and geographical region. Macrovascular complications were determined based on primary care diagnoses (ICD-10 codes) for coronary heart disease (I20, I24, I25), myocardial infarction (I21, I22, I23, I25.2), stroke (I63, I64, G45), peripheral vascular disease (E11.5, E14.5, I73.9) and heart failure (I50). Microvascular complications included retinopathy (E11.3, E14.2), neuropathy (E11.4, E14.4), and nephropathy (E11.2, E14.2, N18, N19). If available, the last HbA1c and the last recorded body mass index (BMI) before index date was also considered in the analysis. Furthermore, lipid disorders, hypertension and related drug treatment were assessed as potential confounders. In addition, the Charlson co-morbidity index was used as general marker of co-morbidity. The Charlson index is a weighted index that accounts for the number and severity of co-morbidities in administrative database studies [10]. The conditions included in the Charlson index cover a wide range of co-morbidities (macrovascular diseases, dementia, pulmonary diseases, gastrointestinal, liver and renal diseases, diabetes, tumors and AIDS).

Descriptive statistics are given for the above-mentioned variables. The analyses of persistence were carried out using Kaplan–Meier curves and log-rank tests separately for BOT and ICT. The median time (days) to discontinuation was assessed. Univariate und multivariate Cox regression models were fitted with persistence as dependent variable and the potential predictors. Stepwise regression models were fitted with type of insulin, age, sex, diabetes duration, diabetologist care, and private health insurance keeping as fixed variables (forced entry). Two sided tests were used and a p-value of <0.05 was considered as statistically significant. All analyses were carried out using SAS 9.3. (SAS Institute, Cary, USA). The analysis was carried out following established national [11] and international