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ORIGINAL ARTICLE

Different Injection Frequencies of Basal Insulins in Type 2 Diabetes Patients under Real-Life Conditions: A Retrospective Database Analysis

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Abstract

Aims:

Little is known about routine use of basal insulins [glargine, detemir, neutral protamine Hagedorn (NPH)] in primary care patients with type 2 diabetes. The aim was to compare injection frequencies of basal insulins in type 2 diabetes in primary care practices, both for basal-supported oral therapy (BOT) and basal–bolus treatment [intensified conventional therapy (ICT)] regimens.

Methods:

Primary care data from 4211 glargine (BOT/ICT, 2247/1964), 1290 detemir (490/800), and 3876 NPH (1331/2425) insulin users were retrospectively analyzed (Disease Analyzer database, May 2009–April 2012). Logistic regression (>1 daily injection) and propensity scores were used to adjust for various confounders (age, sex, type of physician, dosage, body mass index, glycosylated hemoglobin).

Results:

Overall, >1 daily injections were observed in 7.5% of glargine users (BOT, 6.2%; ICT, 9.0%), which was lower than for detemir (overall, 25.4%; BOT, 22.0%; ICT, 27.4%) and NPH (25.4%; BOT, 23.9%; ICT, 27.2%) insulin (all $p < .001$). The adjusted odds of having >1 injection was lower for glargine compared with detemir (odds ratio, 0.26; 95% CI 0.22–0.32) and NPH-insulin (0.20; 0.17–0.23). Similar results were found for BOT or ICT and after propensity score matching.

Conclusions:

Glargine is associated with significantly lower injection frequencies than other basal insulins. These findings might impact patient-reported outcomes, quality of life, treatment satisfaction, and economic aspects of diabetes treatment.

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Abbreviations: (BMI) body mass index, (BOT) basal-supported oral therapy, (HbA1c) glycosylated hemoglobin, (ICT) intensified conventional therapy, (NPH) neutral protamine Hagedorn, (T2DM) type 2 diabetes mellitus

Keywords: injection frequency, insulin therapy, pharmacoepidemiology, primary care

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Introduction

The long-acting insulin analogs glargine and detemir offer advantages over the intermediate-acting human insulins [neutral protamine Hagedorn (NPH)], e.g., they reduce the risk of nocturnal hypoglycemia.[1] In addition, basal insulins differ in their mode of application both in combination with oral antidiabetics or mealtime rapid-acting insulin in type 2 diabetes mellitus (T2DM); glargine is administered once daily, whereas detemir and NPH need to be injected twice daily for equal efficacy.[1] Because of the lower injection frequency, T2DM patients on glargine reported a significantly higher treatment satisfaction compared with NPH insulin.[2] Furthermore, economic advantages for glargine were found from fewer blood glucose measurements and other diabetes-related consumables compared with NPH and detemir.[3,4]

Little is known about routine use of basal insulins (glargine, detemir, NPH) in primary care patients with T2DM. Thus, the aim was to compare injection frequencies of basal insulins in T2DM patients in practices of general practitioners and doctors of internal medicine.

Methods

The Disease Analyzer database (IMS HEALTH) assembles drug prescriptions, diagnoses, and basic medical and demographic data obtained from the practice computer system of general practitioners and specialists throughout Germany.[5] The sampling method for the Disease Analyzer database is based on summary statistics of all doctors in Germany published yearly by the German Medical Association (Bundesärztekammer). The statistical unit of IMS uses these statistics to determine the panel design according to the following strata: specialist group, German federal state, community size category, and age of physician. It has been previously shown that the validity of Disease Analyzer data is sufficient and representative for the general population.[5]

First, all T2DM patients treated with either glargine, detemir, or NPH insulin were identified both for basal-supported oral therapy (BOT) and basal–bolus therapy [intensified conventional therapy (ICT)]; May 2009–April 2012). Mean number of recorded daily injections were analyzed for 4211 glargine (BOT/ICT, 2247/1964), 1290 detemir (490/800), and 3876 NPH (1331/2425) insulin users. The Charlson comorbidity index was used as a generic marker of comorbidity.[6] Logistic regression (>1 daily injection) and propensity scores were used to adjust for confounders (age, sex, practice region, diabetologist care, private/statutory health insurance, daily insulin dosage, comorbidity score). Further adjustment was carried out for body mass index (BMI) and glycosylated hemoglobin (HbA1c) in patients with documented values. Sample size and statistical power were calculated at design stage. Two-sided tests were used and a p-value of <0.05 was considered as statistically significant. All analyses were carried out using SAS 9.2. (SAS Institute, Cary, NC).

Results

The characteristics of the three patient groups are shown in **Table 1**. Overall, glargine users were older than patients with detemir or NPH insulins and received a lower daily insulin dosage ($p < .05$). The physicians treating glargine patients were more often residing in urban regions and in East Germany ($p < .05$). Where no difference was observed between glargine and detemir, NPH insulin users more often had diabetologist care ($p < .05$). Glargine and detemir were prescribed more often in patients with private health insurance. No significant differences were observed for the sex distribution and comorbidity score between glargine users and the other two groups. Mean HbA1c values were slightly higher in detemir than in glargine users ($p < .05$). Finally, the average BMI was significantly higher in NPH compared with glargine users ($p < .05$). Most of these differences were also found for patients with BOT or ICT (**Table 1**).

The injection frequencies for the three basal insulin groups are shown in **Table 2**. The mean number of daily insulin injections was significantly lower in glargine than in detemir or NPH users, irrespective of treatment regimen (BOT, ICT; $p < .05$). Almost all glargine users (93%) received insulin once daily, whereas only 75% of detemir and NPH insulin

Table 1.
Characteristics of Type 2 Diabetes Patients with Prescriptions of Glargine, Detemir, or NPH Insulin in Primary Care Practices: Disease Analyzer, Germany [May 2009–April 2012; Data in Means (Standard Deviation) or proportions (%)]

Variables	Glargine	Total: Detemir	NPH insulin	Glargine	BOT: Detemir	NPH insulin	Glargine	ICT: Detemir	NPH insulin
N	4211	1290	3876	2247	490	1331	1964	800	2545
Age (years)	70.2 (11.3)[a,b]	66.7 (11.7)[a]	69.0 (10.9)[b]	71.1 (11.3)[a,b]	67.1 (11.7)[a]	69.6 (11.2)[b]	68.4 (11.0)[a]	65.7 (11.4)[a]	68.5 (10.8)
Males (%)	51.6	51.1	52.1	51.4	49.3	53.0	51.7	52.2	51.9
Private health insurance (%)	4.9[b]	5.4	2.9[b]	5.7[b]	6.5	3.0[b]	4.1[b]	4.7	2.9[b]
Diabetologist treatment (%)	17.0[b]	16.9	26.5[b]	11.2[b]	12.0	20.0[b]	24.6[b]	20.6	30.3[b]
Region (West Germany) (%)	61.9[a,b]	65.5[a]	62.7[b]	66.8	68.6	69.5	56.6[a]	64.2[a]	58.7
Urban residency[c] (%)	24.4[a,b]	21.1[a]	22.3[b]	26.3[b]	25.6	23.0[b]	22.1[a]	18.1[a]	21.7
Charlson comorbidity score	2.3 (1.6)	2.3 (1.5)	2.3 (1.5)	2.1 (1.6)	2.2 (1.6)	2.1 (1.4)	2.4 (1.6)	2.4 (1.4)	2.3 (1.5)
Daily insulin dosage (IU)	22.7 (14.0)[a,b]	26.0 (17.0)[a]	24.3 (15.9)[b]	20.5 (13.0)[a]	22.7 (14.8)[a]	21.6 (14.9)	25.9 (14.7)[a]	28.5 (18.2)[a]	25.8 (16.1)
HbA1c (%)[d]	7.8 (1.3)[a]	8.1 (1.4)[a]	7.9 (1.3)	7.9 (1.3)[a]	7.8 (1.2)[a]	7.8 (1.2)	7.9 (1.3)[a]	8.2 (1.5)[a]	7.9 (1.4)
BMI (kg/m²)[e]	31.1 (5.6)[b]	31.8 (5.9)	32.0 (5.6)[b]	30.9 (5.5)	31.6 (5.5)	31.6 (5.5)	31.4 (5.6)[b]	32.5 (5.9)	32.3 (5.7)[b]

[a] $p < .05$ glargine versus detemir.
[b] $p < .05$ glargine versus NPH.
[c] >100,000 inhabitants.
[d] Recorded values: glargine $n = 2858$, detemir $n = 937$, NPH $n = 2651$.
[e] Recorded values: glargine $n = 1177$, detemir $n = 381$, NPH $n = 1193$.

Table 2.
Injection Frequencies of Type 2 Diabetes Patients with Glargine, Detemir, or NPH Insulin in Primary Care Practices: Disease Analyzer, Germany [May 2009–April 2012; Data in Means (Standard Deviation) or Numbers and Raw Proportions (%)]

Variables	Glargine	Total: Detemir	NPH insulin	Glargine	BOT: Detemir	NPH insulin	Glargine	ICT: Detemir	NPH insulin
N	4211	1290	3876	2247	490	1331	1964	800	2545
Daily injections	1.08 (0.29)[a,b]	1.27 (0.47)[a]	1.28 (0.51)[b]	1.07 (0.27)[a,b]	1.23 (0.43)[a]	1.25 (0.46)[b]	1.09 (0.31)[a,b]	1.29 (0.50)[a]	1.29 (0.53)[b]
One daily injection, *n* (%)	4167 (92.5)[a,b]	1024 (74.6)[a]	3035 (74.5)[b]	2108 (93.8)[a,b]	382 (78.0)[a]	1014 (76.2)[b]	1789 (91.1)[a,b]	581 (72.6)[a]	1887 (77.8)[b]
Two daily injections, *n* (%)	309 (6.9)[a,b]	330 (24.0)[a]	926 (22.7)[b]	127 (5.7)[a,b]	105 (21.4)[a]	299 (22.5)[b]	164 (8.4)[a,b]	203 (25.4)[a]	569 (23.5)[b]
Three daily injections, *n* (%)	27 (0.6)[a,b]	19 (1.4)[a]	111 (2.7)[b]	12 (0.5)[b]	3 (0.6)	18 (1.4)[b]	11 (0.6)[a,b]	16 (2.0)[a]	89 (3.7)[b]

[a] $p < .05$ glargine versus detemir.
[b] $p < .05$ glargine versus NPH.

had one daily injection. Up to one quarter of detemir and NPH patients had two daily injections, with no differences between BOT or ICT. Three daily injections were rare.

Overall, the multivariable adjusted odds of having more than one daily injection was significantly lower for glargine both compared with detemir (odds ratio, 0.26; 95% CI 0.22–0.32) and NPH (0.20; 0.17–0.23) insulins, respectively. Similar results were found for BOT (glargine versus detemir, 0.23, 0.17–0.32; glargine versus NPH insulin, 0.16, 0.13–0.21) and for ICT (glargine versus detemir, 0.27, 0.21–0.35; glargine versus NPH insulin, 0.22, 0.18–0.27). Among the covariates, diabetologist treatment, higher insulin dosage, and practice region in West Germany were significantly related to an increased odds of having more than one insulin injection ($p < .05$). These results persisted after further adjusting for BMI and HbA1c (data not shown).

Finally, after matching the groups for the propensity score, the odds for more than one injection was also significantly reduced in the glargine group both compared with detemir (odds ratio 0.30; 95% CI 0.24–0.37) and human insulins (0.25; 0.22–0.29).

Discussion

Under real-life conditions, glargine is associated with significantly lower injection frequencies than other basal insulins (detemir, NPH) in T2DM, both in BOT and basal–bolus therapy (ICT). The insulin analogs glargine and detemir have been introduced to improve the limitations of human basal insulins, in particular, inadequate duration of action.[1] Both glargine and detemir are frequently used in combination with oral antidiabetics (BOT) or with rapid-acting insulins. Head-to-head comparisons of glargine and detemir as add-on to oral antidiabetic agents or as basal–bolus therapy showed that similar improvements in glycemic control can be achieved combined with a similarly low risk of hypoglycemia.[7,8] In line with the present analysis, insulin doses were higher with detemir, and it was injected twice daily substantially more often than glargine.[7,8]

The number of daily insulin injections has important economic implications and also has an impact on patient-related outcomes (quality of life, treatment satisfaction) and persistence. The LIVE-SPP study evaluated, from the German statutory health insurance perspective, what costs could be expected in T2DM with glargine- or NPH-based therapies.[3] The total unadjusted annual costs per patient treated with insulin glargine were approximately €195 lower than for a patient with NPH-based therapy.[3] Relevant cost savings between €486 and €684 have also been reported in comparison with detemir.[4,9] The economic advantage of glargine compared with NPH or detemir resulted mainly from a lower resource utilization (dosage, test strips, needles, lancets) related to fewer insulin injections.[3]

Another study in primary care practices in Germany found better patient-related outcomes, including quality of life (Short Form 12 Health Survey, Problem Areas in Diabetes) and treatment satisfaction (Diabetes Treatment Satisfaction Questionnaire, Insulin Treatment Experience Questionnaire) in type 2 patients with glargine compared with NPH insulin.[2] A similar finding has been reported also for type 1 diabetes.[10] In both studies, satisfaction with treatment was most likely to be improved with insulin glargine, because it involves only one injection daily.[2,10]

Persistence with basal insulin therapy, defined as the time period between the initiation and the end of therapy, was also higher for glargine than for other basal insulins.[11,12] Patients on detemir had a higher risk of switching from BOT to ICT than glargine users.[11] Furthermore, the risk of switching to ICT was also significantly higher for patients on NPH insulin (BOT) compared with glargine users.[9] Because ICT is a more complex therapy and is associated with higher risks (hypoglycemia) and costs, these analyses suggest that the use of glargine in BOT has advantages compared with other basal insulins.

It should be noted that retrospective primary care database analyses like the present study are limited by the validity and completeness of data. In particular, no valid information on important outcome measures (e.g., hypoglycemia) were available. Also, assessment of comorbidity relied only on International Classification of Diseases codes by primary care physicians. Finally, BMI and HbA1c values were merely available for a subgroup of T2DM patients.

Moreover, the characteristics of the products may influence the prescription behavior of the treating physicians. Therefore, the populations receiving specific products may differ, which limits comparability. Additionally the frequency of once- or twice-daily administration of the study products may be influenced by the impact of marketing messages and marketing efforts of the manufacturers. There are also strong influences of patients' convenience, economic aspects, reimbursement, and regulatory labeling.

In conclusion, insulin glargine is associated with lower injection frequencies than other basal insulins (detemir, NPH) in T2DM patients in primary care, which may have economic and patient-related (quality of life, treatment satisfaction) implications.

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