Clinical characteristics of type 2 diabetic patients on basal insulin therapy with adequate fasting glucose control who do not achieve HbA1c targets

Manel MATA-CASES,1,2,5 Dídac MAURICIO1,4,5 and Josep FRANCH-NADAL1,3,5

1Jordi Gol Institute for Research in Primary Care (Institut Universitari d’Investigació en Atenció Primària Jordi Gol), 2Primary Health Care Centre La Mina, 3Primary Health Care Centre Raval Sud, Institut Català de la Salut, Barcelona, 4Department of Endocrinology and Nutrition, Hospital Germans Trias i Pujol, Badalona, Spain, and 5Biomedical Research Network in Diabetes and Associated Metabolic Disorders (Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas -CIBERDEM-). Instituto de Salud Carlos III, Madrid, Spain

Correspondence
Josep Franch-Nadal, EAP Raval Sud., Avda. Drassanes 17-21, 08001 Barcelona, Spain.
Tel.: +34 93 3293912
Fax: +34 93 4427763
Email: josep.franch@gmail.com

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Abstract

Background: The aim of the present study was to determine the clinical characteristics of patients with type 2 diabetes mellitus (T2DM) treated with basal insulin who achieved an adequate fasting plasma glucose (FPG) level (<130 mg/dL), but were unable to achieve the HbA1c target (<7%; <53 mmol/mol).

Methods: A cross-sectional study was performed on T2DM patients aged 31–90 years treated with basal insulin registered in the SIDIAPQ primary healthcare electronic database during 2010.

Results: In 2010, of a population of 126 811 T2DM subjects, 9899 were treated with basal insulin (neutral protamine Hagedorn [NPH], detemir, or glargine). Of these, 23.5% (n = 2322) achieved optimal FPG control levels (<130 mg/dL) but an inadequate HbA1c target (>7%). Mean HbA1c values in the controlled and uncontrolled groups were 8.15% (65.6 mmol/mol) and 6.31% (45.5 mmol/mol), respectively. Patients with controlled FPG but uncontrolled HbA1c had longer T2DM duration (11.6 vs 9.9 years), higher systolic blood pressure (138.2 vs 136.3 mmHg) and low-density lipoprotein cholesterol (104 vs 99 mg /dL), and a higher prevalence of retinopathy (24.8% vs 18.2%) than patients (17.8%) with optimal control of both glycemic targets (P < 0.05).

Multivariate analysis showed that inadequate glycemic control was positively related only to younger age.

Conclusion: One-quarter of T2DM patients treated with basal insulin have difficulties attaining the recommended HbA1c goal despite adequate FPG levels. As some guidelines state, healthcare professionals should focus on PPG to identify and intensify treatment to control prandial glucose excursions in these patients.

Keywords: fasting plasma glucose, glycemic control, insulin treatment, type 2 diabetes mellitus.

Significant findings of the study: Half the patients on basal insulin have uncontrolled FPG and HbA1c; hence, adjusting the basal insulin may be a priority. In contrast, when FPG is at target levels but HbA1c remains above target, further interventions to control PPG may become necessary.

What this study adds: It is useful to know the glycemic profile (HbA1c, FPG, and PPG) of T2DM patients to identify those patients needing optimization of the basal insulin dose or intensification with prandial insulin or glucagon-like peptide-1 receptor agonists to control PPG.
Introduction

The prevalence and incidence of type 2 diabetes mellitus (T2DM) are increasing worldwide. Type 2 diabetes mellitus patients have a higher risk of developing microvascular and macrovascular disease than the general population, and the occurrence of these complications depends largely on the degree of glycemic control, as well as on the adequate control of cardiovascular risk factors.

The best index of diabetes control and to prevent T2DM complications is considered to be HbA1c. A good correlation between HbA1c and mean daily glucose concentrations has been observed, confirming that HbA1c is a function of both fasting and postprandial hyperglycemia. For example, the corresponding values of mean blood glucose for HbA1c levels of 6%, 7%, and 8% are 122, 152, and 178 mg/dL, respectively.

The usual target for HbA1c is <7% (≤53 mmol/mol). However, a series of cross-sectional sequential studies performed in Spain have shown that this objective is only achieved by 56%–59% of T2DM patients in primary care. Furthermore, the percentage of patients who reach this objective seems to be notably lower (24%) in the case of less-controlled T2DM patients treated with a combination of insulin and oral agents.

In the treatment of T2DM, the addition of basal insulin to existing oral therapy can help patients attain the recommended glycemic control, mainly because of the effects of insulin on fasting plasma glucose (FPG). Nevertheless, despite established glycemic targets, current elevated HbA1c levels reported in basal insulin-treated patients with adequate FPG (<130 mg/dL) suggest that “real-world” regimens are not optimal and the management of postprandial glucose (PPG) excursions could provide further improvements in glycemic control. Nonetheless, PPG is neither measured routinely nor registered in clinical records. Moreover, with consideration to the importance of glycemic control, recent guidelines established that goals should be individualized based on patient characteristics. In Spain, T2DM patients are generally managed in Primary Care Centers of the National Healthcare System. The common electronic clinical records system allowed us to access data for the entire population registered in the public healthcare system of our region and to determine the actual characteristics of T2DM patients.

Consequently, the aim of the present cross-sectional study was to determine the clinical characteristics of basal insulin-treated T2DM patients treated in primary care centers of the Catalan Health Institute in Catalonia (Spain) who achieved an adequate FPG (<130 mg/dL), but did not achieve the HbA1c target (>7%; >53 mmol/mol).

Methods

The present observational multicenter cross-sectional study of T2DM patients was performed in Catalonia, an autonomous region located in the north-east of Spain, with a population of 7.57 million (in 2012), corresponding to 16% of the total Spanish population. The study was performed by the Catalan Institute of Health (Institut Català de la Salut; ICS), a public entity that provides primary healthcare services to almost 82% of the population registered in this region. In 2012, the ICS managed 288 primary healthcare centers using the same electronic clinical record system (e-CAP; electronic primary care clinical station) in their offices.

Source of information

The data in the present cross-sectional study were obtained from the SIDIAP (Information System for the Development of Research in Primary Care) database of the electronic medical records of all patients attending the primary care practices of the ICS, covering a population of approximately 5.8 million patients (80% of the total population for the region). Detailed information regarding the SIDIAP database (http://www.sidiap.org, accessed 2 January 2016) has been provided elsewhere, and the validity of its information has been analyzed in various studies. Since SIDIAP, a new database has been created that only includes the data recorded by those professionals who attain the highest quality scores in the e-CAP program, namely the SIDIAP database. After the development of a registry quality standard of acute and chronic disease prevalence, patients assigned to professionals with scores above 60% were selected for the SIDIAP database. The SIDIAP database contains data for 1,936,443 patients and was the database used in the present study.

The observation period for the study was the year 2010. The present study was approved by the Ethics Committee of the Jordi Gol Institute for Research in Primary Care (IDIAP).

Patient selection criteria

Live subjects as of the 31st of December 2010, of either gender, aged between 30 and 90 years, diagnosed with T2DM (International Classifications of Diseases (ICD)-10 codes E11, E11.0-E11.9, E14 and E14.0-E14.9) at least 6 months prior to the beginning of the study and who had been treated regularly with any type of basal insulin (Anatomical Therapeutic Classification code A10AC), regardless of the concomitant use of oral antidiabetic drugs, during 2010 were selected for the present study. Patients using premixed or rapid-acting insulin or those...
diagnosed with type 1 diabetes, gestational diabetes, or secondary diabetes were excluded from the study.

Variables analyzed

The primary efficacy variables consisted of FPG and HbA1c values (last value of the previous 15 months), expressed in National Glucose Standard Program/Diabetes Control and Complications Trial (NGSP/DCCT) units. The following data registered at the end of 2010 were collected for each patient: age, sex, diagnosis date, body mass index (BMI), using the most recent weight value of the past 24 months, low-density lipoprotein cholesterol (LDL-C), using the most recent value of the past 15 months, blood pressure (BP; mean systolic and diastolic BP values of the past 12 months), and smoking status, according to the last condition registered.

Data pertaining to chronic microvascular complications were also collected, including diabetic retinopathy, diabetic nephropathy, and impaired renal function. Data were also available for macrovascular complications, including ischemic heart disease, cerebral vascular disease, and peripheral vascular disease. Diagnostic criteria for micro- and macrovascular complications have been described previously.9 Impaired renal function was determined using the last recorded value of the estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease (MDRD) formula (http://www.mdcalc.com/mdrd-gfr-equation/, accessed 2 January 2016) during the past 15 months. Diabetic nephropathy was assessed using the most recent value of the albumin:creatinine ratio in the study period.

Current local guideline targets were used to assess the degree of control,26 namely HbA1c ≤7% (<53 mmol/mol), FPG <130 mg/dL, SBP/DBP <130/80 mmHg, and LDL-C <100 mg/dL for secondary prevention and LDL-C <130 mg/dL for primary prevention. We also assessed these variables according to the pay-for-performance thresholds established by the Institut Català de la Salut, namely HbA1c ≤8% (<64 mmol/mol), LDL-C <100 or <110 mg/dL, and BP<140/90 mmHg.

Statistical analysis

Collected data and determinations were summarized using descriptive statistics. The mean ± SD and proportions were calculated for all variables (clinical characteristics and diabetes-related complications). We always provide the value over the total number of patients, excluding those with missing values. The Chi-squared test and analysis of variance (ANOVA) were used to compare qualitative and quantitative variables, respectively. When significant differences were observed in the quantitative variables, Scheffe’s test was used as a post hoc test to determine the significance of differences among groups at a level of α = 0.05 for all tests.

We used multilevel logistic regression models to identify the factors associated with inadequate HbA1c control (>7%; >53 mmol/mol) in patients with FPG <130 mg/dL, controlling for age, sex, and diabetes duration. Only those variables with a statistically significant effect at the 0.05 level in the univariate analyses remained in the multivariate models. Model 1 was adjusted for age, sex, and diabetes duration; Model 2 included the same variables as Model 1 plus the presence of macrovascular disease; and Model 3 included all variables in Model 2 plus microvascular complications (nephropathy or retinopathy).

Statistical analyses were performed using the Stata Statistical Software, release 11 (StataCorp, College Station, TX, USA). Statistical significance was set at two-tailed P < 0.05.

Results

Of a total population of 1 936 443 individuals between 30 and 90 years of age, 126 811 had a diagnosis of T2DM. Of these, 19 549 (15%) were treated with any type of insulin. Fasting glucose and HbA1c determinations during the study period were not available for 4065 subjects, which led to a study population of 15 484 subjects, of whom 9899 were treated with basal insulin (neutral protamine Hagedorn [NPH], detemir, or glargine; Fig. 1).

Distribution of the study population according to both glycemic targets (FPG and HbA1c) is shown in Fig. 2. Only 17.8% of patients achieved the two optimal glycemic targets, whereas 23.5% of patients achieved optimal FPG control (<130 mg/dL) but an inadequate HbA1c target (>7%; >53 mmol/mol). Most patients (51.3%) did not achieve any of the optimal targets.

Sociodemographic, anthropometric, clinical, and laboratory characteristics of the controlled and uncontrolled HbA1c population in patients achieving the FPG target (<130 mg/dL) are summarized in Table 1. Of the FPG-controlled patients (<130 mg/dL), those who did not achieve the HbA1c target (>7%; >53 mmol/mol) had a longer duration of T2DM (11.6 vs 9.9 years; P < 0.001) and higher mean SBP (138.2 vs 136.3 mmHg; P < 0.001) and LDL-C (104 vs 99 mg/dL; P < 0.001) levels than those patients with HbA1c <7% (<53 mmol/mol). Mean HbA1c values were 6.31% (45.5 mmol/mol) for the HbA1c-controlled group and 8.15% (65.6 mmol/mol) for the uncontrolled group (P < 0.001).
Among the uncontrolled HbA1c patients, those achieving the FPG target (<130 mg/dL) were significantly older, had a longer duration of diabetes, and had lower mean HbA1c, BMI, DBP, and LDL-C values than those who did not achieve the FPG target. The proportion of patients who received some other form of non-insulin antidiabetic drug (mainly metformin) was higher among uncontrolled HbA1c patients (68.2% vs 74.3% for those with FPG <130 and >130 mg/dL).

Figure 1 Flow chart of the study population. T2DM, type 2 diabetes mellitus; FPG, fasting plasma glucose.

Figure 2 Distribution of the overall population according to HbA1c and fasting plasma glucose (FPG) levels.

Table 1 Sociodemographic, anthropometric, clinical and laboratory characteristics of the study population according to the HbA1c targets in patients achieving the target for fasting plasma glucose (<130 mg/dL)

|                     | HbA1c ≤7% | HbA1c >7% | P-value |
|---------------------|-----------|-----------|---------|
| No. subjects (%)    | 1765 (17.8%) | 2322 (23.5%) |         |
| Age (years)         | 71.9 ± 11.1 | 71.9 ± 10.1 | NS      |
| % Men               | 45.8      | 43.5      | NS      |
| BMI (kg/m²)         | 30.3 ± 5.6 | 30.0 ± 5.3 | NS      |
| Diabetes duration (years) | 9.9 ± 7.2 | 11.6 ± 7.6 | <0.001  |
| HbA1c (%)           | 6.31 ± 0.55 | 8.15 ± 0.97 | <0.001  |
| HbA1c (mmol/mol)    | 45.5 ± 3.7 | 65.6 ± 8.2 | <0.001  |
| FPG (mg/dL)         | 96.4 ± 20.9 | 100.5 ± 20.7 | <0.001  |
| SBP (mmHg) (mean)   | 136.3 ± 14.2 | 138.2 ± 13.5 | <0.01   |
| DBP (mmHg) (mean)   | 73.1 ± 8.6 | 73.5 ± 8.5 | NS      |
| LDL-C (mg/dL)       | 99.0 ± 30.8 | 104.0 ± 31.1 | <0.001  |
| Smoking (%)         | 10.8      | 8.9       | <0.05   |

Use of other antidiabetic treatments

- Metformin: 732 (41.3%) vs 948 (40.8%) NS
- Sulfonylurea: 41 (2.3%) vs 72 (3.1%) NS
- Other antidiabetic agent: 64 (3.6%) vs 143 (6.2%) <0.01
- Metformin + sulfonylurea: 76 (4.3%) vs 194 (8.3%) <0.001

Other combinations: 123 (7.0%) vs 228 (9.8%) <0.01

1Unless indicated otherwise, data are given as the mean ± SD or as the number of subjects in each group, with percentages in parentheses.

2BMI, body mass index; T2DM, type 2 diabetes mellitus; FPG, fasting plasma glucose; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low-density lipoprotein cholesterol.

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respectively; \( P < 0.001 \) and among those taking combinations of two or more non-insulin antidiabetic drugs (metformin + sulfonylurea or other combinations; 18.1% vs 23.5% for those with FPG <130 and \( >130 \text{mg/dL} \), respectively; \( P < 0.001 \)).

**Microvascular and macrovascular complications**

Clinical characteristics, including the prevalence of complications associated with T2DM in patients with FPG <130 and \( >130 \text{mg/dL} \) are summarized in Table 2. The prevalence of nephropathy, retinopathy, impaired renal function, ischemic heart disease, and cerebrovascular diseases was significantly different among the two groups \( (P < 0.001) \). No differences were found with regard to peripheral artery disease. Type 2 diabetes mellitus patients with controlled FPG but uncontrolled HbA1c had a higher prevalence of retinopathy (24.8% vs 18.2%) than those with controlled HbA1c, but a lower prevalence of nephropathy (29.1% vs 30.3%), severe renal failure (3.2% vs 5.6%), ischemic heart disease (19% vs 22%), and cerebrovascular disease (12.1% vs 16.5%).

**Age-related differences in cardiovascular risk factors**

The characteristics of patients achieving the FPG target (<130 mg/dL) but with uncontrolled HbA1c in different age groups are given in Table 3. Among this group of patients, younger patients (<65 years) had higher mean HbA1c values, and the prevalence of obesity was higher in the 56–65 year age group. Very poor glycemic control, defined as HbA1c >10%, was particularly elevated in patients <55 years of age (10.2%), but the proportion of patients with very poor glycemic control decreased in the older age groups (Fig. 3). The prevalence of complications associated with T2DM increased with age, with the exception of retinopathy, for which the prevalence was higher in the 56–65 years age group.

Multivariate analyses showed that younger age was the only variable positively related to inadequate glycemic control (HbA1c >7%; >53 mmol/mol) in patients with controlled FPG (<130 mg/dL; Table 4). Sex, duration of T2DM, and microvascular and macrovascular diabetes complications were not positively correlated with inadequate glycemic control.

**Discussion**

Several studies have analyzed the characteristics and degree of control of patients with T2DM in Spain, but the present study is the first to analyze the specific clinical characteristics of T2DM patients treated with basal insulin who, despite adequate basal glycemic control (FPG <130 mg/dL), were unable to achieve the recommended HbA1c target, which was <7% (<53 mmol/mol). The major strength of the present study is the inclusion of every patient with T2DM treated with basal insulin from a total population database of 1 936 443 people. Although the characteristics of the study subjects are similar to previously published data, there was a higher prevalence of older patients with a longer duration of the disease and obesity in the present study.

Similarly to a previous study performed in Catalonia, 15% of T2DM patients in the present study were treated with basal insulin. In Spain, the number of patients receiving insulin treatment varies considerably from one study to another, ranging from 9.6% in some studies up to 30% in others. Among the insulin-treated patients, 24.8% achieved an optimal HbA1c target in the present study, with only 17.8% achieving optimal control of both

| Table 2. Micro- and macroangiopathic complications according to glycemic targets (n = 9899) |
|---|
| **FPG <130 mg/dL** | **FPG ≥130 mg/dL** | **P-value** |
| | Hba1c ≤7% (≤53 mmol/mol) | Hba1c >7% (>53 mmol/mol) |
| | Hba1c ≤7% (≤53 mmol/mol) | Hba1c >7% (>53 mmol/mol) |
| No. subjects (%) | 1765 (17.8%) | 2322 (23.5%) | 733 (7.4%) | 5079 (51.3%) |
| Nephropathy (%) | 30.3 | 29.1 | 25.8 | 30.9 | <0.001 |
| Retinopathy (%) | 18.2 | 24.8 | 19.6 | 18.9 | <0.001 |
| Severe renal failure (%) | 4.7 | 2.6 | 3.7 | 1.8 | <0.001 |
| Ischemic heart disease (%) | 22.0 | 19.0 | 25.0 | 18.4 | <0.001 |
| Cerebrovascular disease (%) | 16.5 | 12.1 | 13.8 | 10.5 | <0.001 |
| Peripheral vascular disease (%) | 10.2 | 9.1 | 10.4 | 8.2 | 0.025 |
| Chronic heart failure (%) | 13.0 | 11.4 | 11.5 | 8.8 | <0.001 |

Nephropathy was defined as an albumin : creatinine ratio >30 mg/g. Severe renal failure was defined using the Modification of Diet in Renal Disease formula as an estimated glomerular filtration rate of <30 mL/min per 1.73 m². FPG, fasting plasma glucose.
glycemic parameters (HbA1c and FPG). Thus, three-quarters of patients show inadequate glycemic control (HbA1c >7% or >53 mmol/mol) and nearly one-quarter of patients do not achieve HbA1c goals despite adequate FPG levels. Therefore, initiation of basal insulin in patients not responding to oral therapy is a successful strategy for some patients, yet a high percentage (75%) does not attain HbA1c <7.0%. Furthermore, in the present study, patients with poor control of HbA1c were more frequently given non-insulin antidiabetic drugs, primarily metformin, which supports the idea that the worst controlled patients receive more complex therapeutic regimens.

In half the patients with uncontrolled FPG and HbA1c on basal insulin, the priority may be to improve glycemic control by optimizing the dose of basal insulin to reach an FPG target of <130 mg/dL. In contrast, when fasting glucose is at target but HbA1c remains above goal, further interventions to control postprandial hyperglycemia may become necessary to achieve HbA1c targets. As far as we know, the present study is the first performed in T2DM patients treated with basal insulin from a population database, and the number of publications available on this issue is scarce. Riddle et al. studied the patterns of hyperglycemic exposure in patients with T2DM, including those who added basal insulin to treatment with oral antidiabetics. In those patients, after intensification of treatment with basal insulin, PPG elevations contributed >60% to hyperglycemia in people with HbA1c >7%. Thus, in individuals in whom basal insulin has been conscientiously titrated, it is the postprandial hyperglycemia that drives the continued elevation of HbA1c levels, regardless of FPG level. Attempts to reduce HbA1c levels in patients with T2DM who still have FPG ≥130 mg/dL by continued increases in the dose of basal insulin may lead to increased severe hypoglycemia.

Table 3 Characteristics of patients treated with basal insulin achieving the target for fasting plasma glucose (<130 mg/dL) but with uncontrolled HbA1c (>7%; >53 mmol/mol) stratified by age (n = 2322)

| Age (years) | % Male | Obese (%) | Diabetes duration (years) | HbA1c (%) | HbA1c (mmol/mol) | HbA1c ≥7.0% (53–63 mmol/mol) | HbA1c ≥8.0% (64–74 mmol/mol) | HbA1c ≥9.0% (75–86 mmol/mol) | HbA1c ≥10.0% (>86 mmol/mol) | ACR >30 mg/g (%) | Renal failure (%) | eGFR <60 mL/min per 1.73 m² | eGFR <30 mL/min per 1.73 m² | Retinopathy (%) | Coronary heart disease (%) | Cerebrovascular disease (%) | Peripheral vascular disease (%) |
|------------|--------|---------|-------------------------|----------|----------------|--------------------------|---------------------------|--------------------------|--------------------------|----------------|----------------|------------------------|-------------------|-----------------|-------------------|-----------------|-------------------|
| ≤55 (n = 153) | 62.7 | 45.9 | 7.8 ± 5.5 | 8.34 ± 1.16 | 67.7 ± 10.3 | 45.1 | 32.0 | 12.4 | 10.5 | 13.5 | 2.9 | 17.0 | 9.1 | 2.6 | 2.6 |
| 56–65 (n = 426) | 53.0 | 52.9 | 10.5 ± 6.4 | 8.24 ± 1.05 | 66.6 ± 9.3 | 50.0 | 28.4 | 14.8 | 6.8 | 22.8 | 7.3 | 29.3 | 13.1 | 7.7 | 8.2 |
| 66–75 (n = 800) | 43.6 | 46.5 | 11.6 ± 6.9 | 8.09 ± 0.96 | 64.9 ± 8.1 | | | | | | | | | | | |
| >75 (n = 943) | 36.1 | 42.9 | 12.5 ± 7.6 | 8.13 ± 0.91 | 65.4 ± 7.6 | | | | | | | | | | | |

1Unless indicated otherwise, data are given as the mean ± SD.
2Obesity was defined as a body mass index >30 kg/m².
3Differences between subgroups by Scheffé’s post hoc analysis.
4ACR, albumin : creatinine ratio; eGFR, estimated glomerular filtration rate.

Figure 3 Distribution of patients with adequate fasting plasma glucose (FPG) levels (<130 mg/dL) but with uncontrolled HbA1c (>7%; >53 mmol/mol; n = 2322).
weight gain compared with those patients who have achieved FPG <130 mg/dL. In such cases, prandial therapy may be necessary. 

Recent guidelines state that reducing PPG values to <180 mg/dL is a reasonable recommendation. Adding one or more injections of rapid-acting insulin with meals is effective for patients with elevated FPG levels, but such an intensification strategy carries the risk of increased hypoglycemia and weight gain, both of which are associated with worse long-term outcomes and would have a detrimental effect in the group of patients with adequate FPG and high BMI. In these cases, another recently available option is combining glucagon-like peptide-1 (GLP-1) receptor agonists with basal insulin, providing complementary actions, lowering both PPG and FPG to improve glycemic control. 

With regard to the importance of glycemic control, recent guidelines established that the goals should be individualized on the basis of the life expectancy of the patient and the presence or absence of comorbid conditions. Therefore, adequate treatment should be considered, particularly in younger T2DM patients, because younger ages were associated with poorer HbA1c control in our patients. Similar to our findings, previous studies confirm the worsening of glycemic control in young T2DM patients, regardless of sex and diabetes complications, and recommend early and aggressive intervention for young patients to prevent long-term complications. Finally, in patients ≥75 years of age with advanced complications or comorbidities, targets should perhaps be more relaxed and an HbA1c <8% (<64 mmol/mol) or even higher in patients on basal insulin may be acceptable. In the present study, 40% of patients were older than 75 years of age and only 48% of them had an HbA1c <8% (>64 mmol/mol); therefore, intensification is probably not necessary for half of them. In the case of patients <75 years of age, one-third of our population, intensification may be necessary in most because of the relatively longer life expectancy and the absence of severe comorbidities in this group. Moreover, decisions regarding objectives have to be made taking into account other variables and the patient should be an active participant in setting goals. 

With regard to the cardiovascular risk factor profile, mean BP and LDL-C values were better than those published in previous Spanish studies, but smoking habits were similar. Controlling these cardiovascular risk factors, especially smoking habits, should be
prioritized in diabetic individuals because of their effects on micro- and macrovascular complications and mortality.\textsuperscript{50,51} Another important finding of the present study is the high number of patients with a BMI $\geq$30 kg/m$^2$ in the subgroup of T2DM patients treated with basal insulin and normal FPG, particularly in the 56–65 year age group (52.9%), a figure that is higher than those found in previous studies\textsuperscript{27,52} and that can also contribute to inadequate control of HbA1c in these patients.

The prevalence of chronic micro- and macrovascular complications was very high in this population of T2DM patients treated with basal insulin. These patients had approximately double the prevalence rates for nephropathy, ischemic heart disease, and cerebrovascular disease and nearly threefold the prevalence of retinopathy, severe renal disease, and peripheral vascular disease compared with rates reported in other Spanish studies that included T2DM subjects.\textsuperscript{9} These results could be explained by a delay in the intensification of treatment, or so-called “therapeutic inertia”, and the fact that therapeutic changes are sometimes introduced after several years of uncontrolled HbA1c.\textsuperscript{33,54} In the setting of primary care in Catalonia, therapeutic inertia has been observed in 30%-40% of patients with HbA1c $>7\%$ (>$53$ mmol/mol)\textsuperscript{55} and treatment modifications are made when HbA1c levels are 1.4 points above the recommended target value of 7\% (53 mmol/mol).\textsuperscript{56}

Patients treated with basal insulin are less controlled and this is probably related to the fact that therapeutic changes are sometimes introduced after several years of inadequate glycemic control. Guidelines propose an early introduction and progression in the combination of drugs\textsuperscript{6,49,57–59} to prevent the worsening of glycemic control, but physicians usually adopt a stepwise approach, which often results in patients spending more than 10 years with an HbA1c $>7\%$ (53 mmol/mol) and 5 years with an HbA1c $>8\%$ (64 mmol/mol) before insulin is started.\textsuperscript{60–62} In patients with high HbA1c on basal insulin but with adequately controlled FPG, the introduction of prandial insulin or a GLP-1 receptor agonist may be appropriate.\textsuperscript{40} The combination of insulin and GLP-1 receptor agonists in obese younger patients could be the best option and may gain the glucose-lowering advantages of both while reducing the risk of hypoglycaemia and controlling body weight.\textsuperscript{40}

Study strengths and limitations

The limitations of the present study are those of any observational study. First, the investigators had no direct access to the individual charts because they were anonymized, making it impossible to verify potential coding errors (type 1 diabetes mellitus instead of T2DM, or vice versa) or the date of diagnosis. Another important limitation of the present study is the lack of data for a significant proportion of patients. For example, one-quarter of patients on insulin were excluded from this study because of the absence of HbA1c or FPG values. Finally, PPG is not routinely registered in the clinical records, and PPG levels as a possible explanation for the increase in HbA1c when FPG is well controlled therefore cannot be assessed in the present study because of its design. Finally, our population belongs to a specific Mediterranean area and is mostly Caucasian; therefore, the results may not be applicable to other populations.

Conclusion

The data suggest that, in T2DM patients, basal insulin treatment results in a very limited control of the established glycemic targets, especially in this group of patients with high cardiovascular risk and for whom improving glycemic control is mandatory. One-quarter of T2DM patients treated with basal insulin do not reach the recommended HbA1c goal despite normal FPG levels, and multivariate analysis showed that inadequate glycemic control was positively correlated only with younger age. Based on these data, achieving the current FPG goal of $<130$ mg/dL may not be enough to reduce the risk of complications in patients with T2DM treated with basal insulin and high HbA1c levels. As some guidelines state, in addition to the control of other cardiovascular risk factors, healthcare professionals should focus on PPG to identify and intensify treatment to control prandial glucose excursions in these patients.

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Disclosure

None declared.
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