Glycemic Control and Hospital Admission Risk in Type 1 Diabetes is Related to the Use of Carbohydrate Counting and Frequency of Self-Monitoring of Blood Glucose: RSD1 Study

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Abstract

Introduction and objectives: Diabetes mellitus type 1 (DM1) represents 5–10% of the total prevalence of diabetes. Few studies exist to demographically and clinically describe DM1.

Subjects and methods: observational, cross-sectional study of patients with DM1 over 14 years of age treated by hospital endocrinologist.

Results: 221 patients (104 men, 37.5 ± 12.7 years) from seven hospitals. Caucasian 97%; Education: primary 22.7%, secondary 48.5%, university 25.3%. Anthropometric data (average ± SD): Weight 70.1 ± 13.7 kg; Height 166.5 ± 8.8 cm; BMI: 25 ± 3.8 kg/m²; Waist circumference: 87.3 ± 18 cm. Family history: DM (46.3%, DM1 28.3%, DM2 71.7%), thyroid disease (17.6%), early CVD (6.5%), Active smoker 20%, ex-smoker 18.6%. DM1 duration: 15.8 ± 10.2 years. Treatment: basal + bolus 74.7%; premixed insulin: 5.7%, basal 2.7%, CSII: 17.1%; metformin: 8.5%; Self-monitoring of blood glucose (SMBG) frequency: 3.6 ± 1.4 times/day; Uses insulin/carbohydrates ratio: 38.8%; regular physical activity: 55.6%; Lipid-lowering drugs: 29.1%; antihypertensive agents: 23.5%. Metabolic control: HbA1c = 7.7 ± 1.3% (61 ± 9 mmol/l); Poor adherence to diet (p < 0.001), number of SMBG (p < 0.01) and regular physical activity (p < 0.05) explains 34.2% of the changes in Hb1Ac. Risk of hospital admission is reduced with the use of carbohydrate counting (OR 0.39, p = 0.002) and with the largest number of blood glucose controls (OR 0.65, p = 0.007).

Conclusions: More efforts are necessary to improve the overall metabolic control of patients with DM1. Epidemiological studies aimed at DM1 populations are necessary in order to define the necessary resources.

Keywords: Type 1 Diabetes; Epidemiology; Therapeutic education; Insulin therapy; Complications of diabetes

Introduction and Objectives

Diabetes mellitus (DM) is defined as hyperglycaemia due to insufficient secretion of insulin, inadequate action of the same or both causes. Treatment of diabetes implies the need for changes in lifestyle (diet, exercise), administration of drugs and/or insulin and monitoring of blood glucose. In addition, patients with diabetes may be at increased risk or predisposition to develop macrovascular complications (ischemic heart disease, stroke, lower limb ischemia) and microvascular complications (retinopathy, nephropathy and neuropathy) [1-3].

DM groups a broad list of different diseases among which two clinical conditions are the main ones: Type 1 (DM1) and type 2 diabetes (DM2). They differ in their epidemiological, clinical, genetic and immunological characteristics, as contained in multiple reports, including most notably the WHO report of 1985 [4] and the consensus document for the care of people with DM in Spain [5].

DM is a chronic disease with a high prevalence. It affects 13.8% of the Spanish adult population [6]. The prevalence of DM1 has been estimated at between 0.08 and 0.2% [7]. A recent study carried out in Castilla y León estimated the incidence of DM1 in 10.8 cases/100,000 inhabitants/year in people under 15 years of age [8].

To reduce the complications associated with DM1 is essential to maintain good glycaemic control [9]. In the study Diabetes Control and Complications Trial (DCCT), intensive treatment reduced the overall risk of retinopathy by 76%, proliferative or severe non-proliferative retinopathy by 47%, microalbuminuria by 39%, macroalbuminuria by 54% and the risk of clinical neuropathy by 60% [10,11]. These results led the American Diabetes Association (ADA) to intensify the objectives of glycaemic control of DM, recommending a fasting blood glucose of 90–130 mg/dl and glycated haemoglobin A1c (HbA1c) < 7% [12]. Individually this HbA1c goal may be 6.5%. A large number of people...
with DM1 are young people/adults without other complications, therefore an HbA1c <6.5% goal would be applicable.

DM1 patients are dependent on exogenous insulin to regulate blood sugar levels. The current strategy to obtain glycaemic control is to imitate physiological insulin secretion. For this, the most used regimen is that of multiple daily insulin (MDI) in basal-bolus strategy. This regimen requires administration of basal insulin, characterised by a serum insulin concentration profile which remains as stable as possible over a period of 24 hours, and additional injections of rapid-acting insulin before meals. In addition, insulin administration is possible by means of the use of continuous subcutaneous insulin infusion (CSII) pumps.

Individuals with DM1 must adjust their insulin treatment according to the amount of carbohydrates ingested, therefore carbohydrate counting is basic [12,13]. Also, daily adjustment of the insulin treatment in DM1 requires the frequent use of self-monitoring of blood glucose (SMBG). The ADA recommends that patients with MDI or CSII make at least 3 daily SMBG (before meals) and, occasionally, postprandial, before going to bed, before exercise, when they suspect hypoglycaemia, after treating hypoglycaemia and before critical actions such as driving [12]. In the last 15 years, systems for continuous glucose monitoring (CGM) have been launched to the market. Persons with DM1 are the first candidates for using this new technology. The development of insulin pumps integrating CGM makes them even more suitable for patients using CSII. Some circumstances besides reimbursement policy hinder a more widespread usage of CGM [14].

Multiple factors exist that can influence the control of DM1, including demographic and psychosocial factors such as age, motivation, compliance, diabetes education and abilities for handling the disease.

Unfortunately, the limited data in this population may influence an insufficient allocation of human and financial resources in their care. At the Diabetes Work Group of the Society of Endocrinology, Diabetes and Nutrition for Castilla y León (SCLEDyN) we set out to describe a representative sample of patients with DM1 followed in our consulting rooms.

Materials and Methods

Design

Descriptive observational study: Data collected through the Type 1 Diabetes Registry of the Diabetes Group of the Sociedad Castellano Leonesa de Endocrinología Diabetes y Nutrición (SCLEDyN) (RSD1). This registry is carried out in Endocrinology Units of Hospitals in Castilla y León from January 2011 using a Web portal created for this purpose. The data are obtained from the clinical history of patients who attend Endocrinology Consultations and are introduced by the endocrinologists of the Diabetes Group of SCLEDyN (a representative in each hospital of the region).

Study classified by the AEMP’s (Spanish Agency for Medicines and Health Products) on 24 May 2012 and accepted by the Clinical Research and Ethics Commission of the Hospital General de Segovia.

Study population

People with DM1 over 14 years of age followed up in Endocrinology consultations. For this study all those included in the RSD1 registry until June 2014 have been analysed. The official population of Castilla y León was 2,546,078 inhabitants (01/01/2012), therefore we considered a prevalence of DM1 (x 0.1%) of 2,547 patients. A representative sample of the population with DM1 over 14 years of age from the autonomous community was considered as 227 subjects. Once this sample size was obtained, the case data included were consecutively analysed with a representation sufficient and proportional to the size of the population of the health areas of the region.

Analysed variables

- Sociodemographic variables: present age, sex, ethnic group and self-declared education level (in 4 categories: no studies, primary studies, secondary studies, university studies).
- Anthropometric variables: weight, height, BMI, waist circumference, systolic arterial pressure (SBP) and diastolic arterial pressure (DBP), heart rate.
- Clinical variables: Personal and family history, age at diagnosis of diabetes, toxic habits, presence of hypertension (HT) and use of antihypertensive drugs, dyslipidemia and use of lipid-lowering drugs, associated autoimmune diseases, diagnosis of complications associated with diabetes (nephropathy, neuropathy, retinopathy, cerebrovascular disease, ischemic heart disease, heart failure, arrhythmias, etc.), hospital admissions.
- Descriptive treatment variables: type of insulin and method of administration (basal-bolus, continuous subcutaneous insulin infusion [CSII]), use and amount of corrective insulin, use of oral agents, use and frequency of self-monitoring of blood glucose, adherence to diet plan (referred by the doctor), use of carbohydrate count (self-reported) and insulin/serving ratio used, frequency of analytical control, physical activity (self-reported, physical activity is considered an average of more than 30 minutes a day).
- Analytical variables: glycated haemoglobin (Hba1c), average of 3 blood glucose profiles at 6 points (before and two hours after breakfast, lunch and dinner), creatinine, creatinine clearance (Cockroft-Gault formula), uric acid, total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides, liver transaminases, TSH, autoimmunity markers.
- Estimation of overall cardiovascular risk: Two scoring systems have been applied for calculation of overall cardiovascular risk: Framingham [15] and SCORE (Systematic Coronary Risk Evaluation)[16].

Statistical methods

Quantitative variables were described with centralisation and dispersion measurements (mean, standard deviation [SD]), median, minimum, maximum, N [valid] and confidence intervals [CI] at 95%). The qualitative variables were described by means of the absolute and relative frequencies. Several models of univariate and multivariate logistic regression have been made to consider the influence of different clinical and demographic variables in health results. It was verified that the models fulfil the criteria of normality and homogeneity of variance and that there is no collinearity between the variables. The data were analysed using SPSS v.17.0.

Results

The number of patients included was 221, with a total of 216 patients evaluated.
Demographic data

Table 1 summarises the demographic data of the sample. The studied population included 102 men (47.2%), 209 Caucasian (97.2%). The average age was 37.7 ± 13 years. 73.8% have secondary studies (48.5%) or university studies (25.3%).

Personal and family history

20% are smokers and another 18.6% are ex-smokers. 55.6% practice regular physical activity (more than 30 minutes/day). It is considered that 69% adhere to the recommended diet plan (Table 1).

46.3% present family history of DM (28% of them DM1, n=28), 17.6% thyroid disease (13.9% hypothyroidism and 3.7% hyperthyroidism).

Anthropometric data

The physical examination data are described in Table 1. It is verified that the BMI globally classifies this young population (average 38 years old) as overweight.

Characteristics of diabetes and comorbidities

The average time from diagnosis of diabetes to the visit date was 15.8 ± 10.2 years, with a minimum of 1 year and a maximum of 54 years.

Table 2 gathers the prevalence of comorbidities present in the sample.

The univariate logistic regression analysis indicated that the presence of chronic complications was associated with the duration of diabetes: nephropathy (OR 1.08, CI 95% 1.04–1.12, p < 0.001), neuropathy (OR 1.11, CI 95% 1.06–1.17, p = 0.001), retinopathy (OR 1.16, CI 95% 1.10–1.23, p < 0.001). In the case of nephropathy and neuropathy (OR 1.11, CI 95% 1.06–1.17, p = 0.001), retinopathy (OR 1.16, CI 95% 1.10–1.23, p < 0.001).

Nevertheless, in the multivariate analysis only the duration of the diabetes continues to be a predictor of the three chronic complications most prevalent in DM1: nephropathy (OR 1.09, CI 95% 1.05–1.14, p < 0.001), neuropathy (OR 1.18, CI 95% 1.07–1.30, p = 0.001) and retinopathy (OR 1.16, CI 95% 1.10–1.23, p < 0.001).

61.1% had been admitted to hospital: 77.4% for metabolic decompensation, 5.3% of them were hypoglycaemia. On average each patient was admitted 1.5 ± 1.8 times for hyperglycaemic decompensation and 1.7 ± 1.9 times for hypoglycaemia. Very interestingly, the risk of hospitalisation is significantly reduced statistically with the use of advanced basal-bolus therapy (carbohydrate counts) (OR 0.39, CI 95% 0.21–0.71, p = 0.002) and with the largest number of blood sugar controls carried out (OR 0.65, CI 95% 0.48–0.89, p = 0.007).

Regarding the presence of other autoimmune diseases, 33% had been diagnosed with autoimmune hypothyroidism, 1% with autoimmune hyperthyroidism, 1.4% with vitiligo and 1.9% with coeliac disease.

Metabolic control of diabetes

The average HbA1c was 7.7 ± 1.3% (4.8–14.3), percentage of patients with HbA1c < 7%: 23.1% (confidence interval (CI) at 95%: 17.7–29.5).

The remaining laboratory data is included in Table 3.

The logistic regression model describes 8 factors that have significant univariate relation to the Hb1Ac value. Poor adhesion to diet (R² = 0.183, P < 0.001) increases Hb1Ac. On the contrary, university studies (R² = 0.015, P = 0.032), regular physical activity (R² = 0.083, P < 0.001), the use of CSII (R² = 0.139, P = 0.019), the use of carbohydrate counts
Lispro 20.5 ± 10.6; Aspart 21.3 ± 12.5; Glulisine 19.5 ± 10.8; Regular (R2 = 0.161, P < 0.001) and a greater number of controls (R 2 = 0.135, P < .01) and regular physical activity (B = 0.468; P < .05). The model explains 34.2% of the changes in Hb1Ac values. The first predictor explains 22.7%, the second adds 9% and the third 2.5%.

Estimation of overall cardiovascular risk

Two scoring systems have been applied for calculation of overall cardiovascular risk at 10 years: Framingham [15] and SCORE (Systematic Coronary Risk Evaluation) [16]. The average results for the sample are 2.3 ± 1.8% and 0.6 ± 1.6%, respectively.

Treatment

89.2% had received diet instructions. 98% carried out self-monitoring of blood glucose (SMBG) with an average frequency of 3.6 ± 1.4 controls/day. 97% carried out regular HbA1c controls (minimum 2/year).

Insulin treatment is detailed in Table 4. 73% use corrective doses of insulin (average dose 1 IU/53 mg/dl of blood glucose on target). 35.7% use insulin/ratio ratio (n = 76). In these cases the average dose is 1.2 ± 0.5 insulin units per carbohydrate ration. Both the corrective dose and the insulin/exchange ratio are among those regularly recommended. 12.5% used CSII. No patient regularly used CGM. The number of daily injections (average ± SD) for different insulin was: Glargin 1.1 ± 0.3 (8.3% 2 daily doses); Detemir 1.4 ± 0.5 (36.4% 2 daily doses); NPH 2.2 ± 0.6 (14% 1 injection, 57% 2 injections, 29% 3 injections). Lispro 2.9 ± 0.3; Aspart 2.9 ± 0.4; Glulisine 2.8 ± 0.5; Regular 2.5 ± 0.9. The total daily administered dose (average ± SD) (IU): Glargin 24.7 ± 10.4; Detemir 31.6 ± 15.5; NPH 36.7 ± 21.8; Lispro 20.5 ± 10.6; Aspart 21.3 ± 12.5; Glulisine 19.5 ± 10.8; Regular 26.0 ± 12.1. The total daily dose of insulin in relation to body weight was 0.69 (0.62–0.89) IU/kg. The percentage of human insulin use is low (8% of NPH as slow acting insulin and 3.8% of regular as fast acting insulin). 8.5% use metformin. Other medications include: antiplatelet drugs (17.3%), lipid-lowering drugs (29.1%), antihypertensive drugs (23.5%, of which: ACEI 54%, ARA2 34%).

Discussion

DMI assumes a significant percentage (5–10%) of a highly prevalent disease such as DM. Its aetiology (autoimmune destruction of insulin-producing cells) forces the monitoring of a complex hormone replacement therapy consisting of administering subcutaneous insulin injections daily or using devices such as CSII. Usually DMI is diagnosed in childhood or youth, therefore this treatment lasts almost a lifetime.

The sample collected (average age 38 years) is socially representative of the middle-aged population of our community [17] and reflects a population with a significantly higher level of education (74% with secondary or higher education). This variable was associated with better blood glucose control. Also a satisfactory frequency of medical visits is noted (97% more than 2 per year). However, monitoring data and health outcomes are far from the optimal target: average HbA1c is 7.7%, only 21% of them below 7% and almost 50% have required hospitalisation due to metabolic decompensation. The predictive analysis confirms that the use of an advanced treatment (CSII, basal-bolus advanced, greater frequency of self-monitoring) is associated with better metabolic control.

Regarding the prevalence of chronic complications (nephropathy 16%, neuropathy 12% and ophthalmopathy 24%) our sample with an average duration of almost 16 years shows differences with other national and foreign studies. One held in Catalonia with DMI patients after 14 years of follow-up showed a prevalence of nephropathy 9.4%, neuropathy 21% and ophthalmopathy 19% [18]. In prospective reference studies such as DCCT/EDIC the data are different. A review of the long-term (30 years) results of the intensive treatment intervention vs. conventional DCCT study and its subsequent EDIC follow-up study [19], DCCT (12.3 years duration of DMI) describes the prevalence (intensive vs. conventional) of nephropathy 10.2 vs. 17.8%, neuropathy 9.3 vs. 17.5% and ophthalmopathy 71.7 vs. 82.7%. In the case of the EDIC study (18 years duration of DMI) these data are nephropathy 18.5 vs. 24.9%, neuropathy 23.6 vs. 32.7% and ophthalmopathy 89.3 vs. 95.3%. However, these data are difficult to compare to ours because of the different screening methods and diagnostic criteria used. The

<table>
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<tr>
<th>% patients</th>
<th>Number of injections/day</th>
<th>Average daily dose</th>
<th>Average daily dose of %</th>
<th>(of weight/day)</th>
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<tr>
<td><strong>Basil + bolus</strong></td>
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<tr>
<td>Glargine</td>
<td>56.3 (120)</td>
<td>1.1 ± 0.3</td>
<td>24.7 ± 10.4</td>
<td>/0.35</td>
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<tr>
<td>Detemir</td>
<td>10.3 (22)</td>
<td>1.4 ± 0.5</td>
<td>31.6 ± 15.5</td>
<td>/0.45</td>
</tr>
<tr>
<td>NPH</td>
<td>8 (17)</td>
<td>2.2 ± 0.6</td>
<td>36.7 ± 21.8</td>
<td>/0.52</td>
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<tr>
<td><strong>Fast acting insulin</strong></td>
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<tr>
<td>Lispro</td>
<td>23.9 (51)</td>
<td>2.9 ± 0.3</td>
<td>20.5 ± 10.6</td>
<td>/0.29</td>
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<tr>
<td>Glulisine</td>
<td>11.3 (24)</td>
<td>2.8 ± 0.5</td>
<td>19.5 ± 10.8</td>
<td>/0.27</td>
</tr>
<tr>
<td>Regular</td>
<td>3.6 (8)</td>
<td>2.5 ± 0.9</td>
<td>26.0 ± 12.1</td>
<td>/0.37</td>
</tr>
<tr>
<td>CSII</td>
<td>12.5 (27)</td>
<td></td>
<td>43.7 ± 22.8</td>
<td>/0.68</td>
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<tr>
<td><strong>Mixtures</strong></td>
<td>2.8 (5)</td>
<td>2.75 ± 0.4</td>
<td>61.6 ± 29.7</td>
<td>/0.79</td>
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Table 4: Insulin treatment.
highest prevalence of chronic complications in prospective studies, especially retinopathy and neuropathy, also suggest shortcomings in the screening of complications conducted in clinical practice.

Data concerning the treatment identify some possible areas for improvement. The percentage of CSII users (12.5%) is low compared with other countries, something common with the rest of Spain and that is subject to controversy in its explanation [20,21]. In addition, in this sample there continues to be a significant number of patients treated with premixed insulin (2.8%), a treatment not recommended for people with DM1.

Other data are perhaps more interesting to try to describe to what extent the treatment used is really an advanced treatment with self-monitoring. Our regression analysis indicates that HbA1c depends on the SMBG frequency. A recent study has once again confirmed that the number of daily blood glucose controls in people with DM1 is clearly correlated with the degree of blood sugar control, showing that participants who did SMBG 3–4 times a day had an average HbA1c of 8.6% compared with an HbA1c of 7.6% among those who did so more than 10 times a day [22]. In our study the SMBG average was 3.6. Nevertheless our average HbA1c was 7.7%. It is likely that the populations and methodology used in each study can explain the differences. Regardless of the difference of the SMBG/HbA1c relation in either study, the average number of daily controls is less than would be desirable.

The use of systems for CGM would also be of interest in this population. It can complement SMBG adding comprehensive and dynamic information on glucose profiles including real-time alarms. However, CGM systems are not reimbursed in this region. This issue, besides other reasons depending on both on the health providers and the people with DM1, are major obstacles facing a more widespread usage of CGM [14]. CGM efficiency and cost-effectiveness in DM1 has been positively evaluated [23-25].

Also the percentage of patients (35.7%) who perform carbohydrate counts and use a sensitivity factor or insulin/exchange-ratio ratio and those that use corrective doses of fast acting insulin (63.4%) could improve. A recent systematic review and meta-analysis has confirmed the effectiveness of carbohydrate counting in DM1 [26]. These data indicate an opportunity to improve the application of advanced insulin regimes and possibly diabetes education shortfalls that should be addressed.

Our study reveals the frequency of hospital admissions for acute decomposition of DM and confirms that this rate can be reduced with the use of advanced basal-bolus therapy (counting carbohydrates) and with more blood sugar controls carried out. The cost of a hospital admission for hypoglycaemia in Spain is set at €2,478 [27] and €702 for hypoglycaemia treated by the emergency services [28]. The application of welfare strategies and therapeutic education could reduce these events (potentially fatal) and their associated cost [29].

With regard to the type of insulin used, the percentage of human insulin use is low (8% of NPH as slow acting insulin and 3.8% of regular as fast acting insulin). The total amounts of insulin (0.69 IU/kg) and those corresponding to each type of insulin are consistent with previous data, with the detemir dose being 30% greater than glargine (31.6 vs. 24.7 IU/day) and human insulin doses higher than those of similar insulin [30,31]. The use of detemir insulin requires 2 injections in a greater number of patients (36.4%) than those using glargine (8.3%), which is also described in previous studies [30,31].

Our data describes the blood glucose profile provided by DM1 patients studied. The average (144.8 mg/dl) is lower than the expected average value of HbA1c (7.7%), which should be around 175 mg/dl, in agreement with the estimates of Nathan et al. [32]. This data could confirm the impression of the professionals that the profiles provided by the patients usually represent days of better control and not the complete profile of the patients. However, the author has empirically analysed SMBG data in different HbA1c ranges, concluding that the objectives of the desirable daily blood glucose profile in a realistic clinical setting may be different from those proposed by the clinical guidelines [33]. Specifically, an average blood sugar profile (before and after breakfast, lunch and dinner) for an HbA1c between 6.5 and 7% would be: 142–177 127–158 145–159; not very different from that provided by our patients (137–151 137–153 148–143).

Finally, data describing the degree of personal adherence and healthy lifestyles of people with DM1 remain striking, 20% of patients continue smoking and 45% remain sedentary. Additional measures of behavioural change may be necessary to change this situation.

In conclusion, the data of this study suggest that more efforts are necessary to optimise the overall metabolic control of patients with DM1. Epidemiological studies aimed at populations of people with DM1 are necessary in order to define the resources necessary to reduce complications associated with DM1 and improve the quality of life of those affected.

Acknowledgment

This work has received economic aid from Sanofi Diabetes for the development of an online data collection tool. The statistical analysis was performed by José-Manuel García de Cecilia (3datos statistical processing), sponsored by the Research Commission of Hospital General de Segovia.

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