A Retrospective Study in 5,989 Patients with Type 1 Diabetes in 10 Outpatient Diabetic Clinics in Sweden of the Frequency of Measuring HbA1c in Clinical Practice

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Abstract

Aim: Guidelines for the treatment of type 1 diabetes generally recommend quarterly or more frequent Haemoglobin A1c (HbA1c) assessment in patients with inadequate glycaemic control. The purpose of the current study was to evaluate to what extent these guidelines are followed in clinical practice in Sweden.

Method: We studied 5989 patients with type 1 diabetes from 10 outpatient diabetes clinics in Sweden from 1 January 2005 to 31 December 2009. Data on HbA1c measurement frequency were obtained from the Diab-Base electronic medical records database, where HbA1c measurements are recorded together with other patient characteristics, including treatment and other general risk factors for diabetic complications. The frequency of HbA1c measurements was obtained for all patients by calendar year, care unit, and during time periods where glucose was classified as well controlled (HbA1c<=7.0%) or inadequate (HbA1c 7.0% or higher).

Results: The mean annual number of HbA1c assessments when glucose control was inadequate was 1.83 compared with 1.58 during well controlled time-periods. In 35.4% of cases the next HbA1c check following an HbA1c >7% was performed within 4 months. The probability of a subsequent assessment in the 4 months following an HbA1c value>7.0% increase in patients treated with continuous subcutaneous insulin infusion (CSII), OR=1.57 (1.46-1.69). Differences were also noted by care unit, age, gender, glycaemic control, calendar year, and weight and diabetes duration.

Conclusion: In patients with type 1 diabetes, HbA1c is measured less frequently in clinical practice in Sweden than guidelines recommend, although patients with CSII and treated in certain care units receive more frequent assessments.

Keywords: Type 1 diabetes mellitus; HbA1c; Diabetic complications; Insulin pump; Availability; Diabetes care

Background

Diabetes mellitus remains a growing public health problem. There are approximately 385 million people worldwide with diabetes (types 1 and 2), and the prevalence is predicted to rise to 500 million by 2030 [1]. The prevalence of type 1 diabetes mellitus is highest in Scandinavian countries and has increased in several countries during the last decades [2-4]. The costs associated with diabetes account for more than 10% of the entire European health budget, with diabetes complications accounting for a major part of these costs [5,6].

Good glycaemic control is crucial in preventing complications in patients with type 1 diabetes [7,8]. Recommended therapy for obtaining good glycaemic control is intensive therapy including multiple daily doses of insulin, frequent blood glucose measurements, and regular Glycosylated Haemoglobin (HbA1c) monitoring [7,9-12]. Currently, less than 20% of adult type 1 diabetic patients in Sweden achieve good glycaemic control (<7.0%), and around 25% have very poor glycaemic control (>8.6% [13]), as poor as when patients in studies have received only basal insulin once or twice a day without any prandial insulin [7]. In Sweden, patients with type 1 diabetes have free access to novel insulin analogues, self-measurement of blood glucose (glucose-monitoring strips and meters), HbA1c tests, while insulin pumps are reimbursed when glycaemic control is inadequate.
Since many patients with type 1 diabetes in Sweden have poor glycaemic control, despite the widespread availability of novel treatment strategies, it is possible that barriers exist achieving adherence with blood glucose measurements, achieving proper insulin dosing, or providing basic diabetes care.

To support the intensive treatment strategy, diabetes guidelines generally recommend visits to a diabetes educator or physician with HbA1c monitoring performed at least every third month in patients with inadequate glycaemic control [9-12]. To our knowledge there are few studies examining adherence to these guidelines in clinical practice. Therefore, we examined the frequency of visits to 10 outpatient diabetes clinics in Sweden that included HbA1c checks over a 5-year period and evaluated potential explanatory factors for more frequent glycaemic monitoring.

**Methods**

**Data source**

Data were obtained from an electronic medical records system (Diab-Base, Journalia AB, Sweden), which is used at 10 hospital-based diabetes clinics that treat adult outpatients (18 years or older) in Sweden [14]). Most clinics in Sweden have used Diab-Base since the year 2000. The system has been described in detail and has been used in several studies of diabetes treatments among patients with both types 1 and 2 diabetes [14-18]. Briefly, the system includes information about risk factors, treatment, and complications that are recorded during clinical visits. All risk factor measurements, such as HbA1c, blood pressure, blood lipids, body mass index (BMI), type of diabetes, and insulin dose, are tracked electronically. In addition, type of insulin delivery, either continuous subcutaneous insulin infusion (CSII) or Multiple Daily Injections (MDI) can be tracked electronically, as along with information on diabetic complications.

**Current cohort and data analysis**

The current cohort included patients with type 1 diabetes studied from January 2005 to 31 December 2009. The frequency of HbA1c measurements was assessed for all patients, as well as by calendar year, diabetes outpatient clinic (also further on denoted care unit), and period of time when patients achieved good (HbA1c ≤ 7.0%) and inadequate glycaemic control (HbA1c>7.0%). Potential predictors for receiving a subsequent HbA1c check within 4 and 7 months after an HbA1c value >7.0% were examined, including age, sex, type of insulin delivery (MDI or CSII), diabetes duration, HbA1c level, weight, BMI, insulin dose (U/kg), and care unit.

**Statistics**

The mean number of HbA1c checks for the entire cohort was calculated as the mean value resulting from the annual means of all HbA1c checks for each individual patient. The mean number of HbA1c checks during periods with an HbA1c>7.0% was calculated with the corresponding methodology during the periods of time when an HbA1c>7.0% was identified until a subsequent check identified a novel value ≤7.0%. The corresponding methodology was similarly used to estimate the mean number of HbA1c checks during patient periods with HbA1c ≤ 7.0%.

To predict the likelihood of having an HbA1c check in 4 and 7 months following an HbA1c>7.0% at any time during the study,

Generalized Estimating Equations (GEE) models with a compound symmetry covariance matrix were used to allow for adjustment of within-individual correlations [19]. Univariate GEE models were used to identify the statistically significant predictors that affected the outcome.

Stepwise logistic regression was used for selection of independent predictors that were statistically significant. Once variables were selected, the GEE models were performed including the selected variables to obtain the adjusted odds-ratios (OR), 95% Confidence Intervals (CI) and associated p-values. Imputation of missing weight, BMI, and insulin doses was performed by using last observation carried forward. All tests were two-tailed and conducted at the 0.05 significance level.

**Results**

In total, there were 5,989 patients with type 1 diabetes evaluated. Patient characteristics for the whole cohort at first visit during the years 2005 to 2009 as well as in relation to the number of annual HbA1c measurements are presented in Table 1a. Distribution of mean number of annual HbA1c measurements by care unit is given in Table 1b.
Table 1a: Patient characteristics at first visit during years 2005 and 2009 in DiabBase in total and in relation to the number of annual HbA1c measurements performed during years 2005-2009 by care unit.

Table 1b: Distribution of mean number of annual HbA1c measurements performed during years 2005-2009 by care unit.

The mean annual number of HbA1c measurements increased moderately, from 1.72 in 2005 to 1.90 in 2009, with a mean of 1.78 over the study period (Table 2). There was an increase p<0.0001 in the mean HbA1c level, from 7.92% in 2005 to 8.05% in 2009 (Table 2). The proportion of patients reaching a target HbA1c of ≤ 7.0% varied, from a low of 18.6% in 2009 to a high of 22.9% in 2007 (Table 2).

Table 2: Distribution of number of yearly visits, HbA1c levels and HbA1c <=7 (%) by calendar year.

The mean age of patients with 3 or more HbA1c checks per year was 37.4 years, compared to 42.9 years for the entire cohort. Females comprised 44.4% of the entire cohort, compared to 51.8% and 49.5% among patients with 3 to 4 annual HbA1c checks and 4 or more annual HbA1c checks, respectively, p=0.0022 for test between ≥3 vs. ≥4 HbA1c checks. Diabetes duration was 20.9 years among the entire cohort, compared to 15.9 and 15.8 years, respectively, in patients with 3 to 4 and 4 or more HbA1c checks per year, p<0.0001 for test vs.<3 HbA1c checks. Among the entire cohort, 21.1% had CSII, compared to 39.9% and 37.1%, respectively, in patients with 3 to 4 and 4 or more annual HbA1c checks, p<0.0001 for test vs.<3 HbA1c checks. In unit 10 there were 36.2% of patients having 3 or more HbA1c checks per year, p<0.0001 for test vs.<3 HbA1c checks, whereas fewer than 10% of patients had 3 or more annual HbA1c checks in most other care units (Table 1b).

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and 1.50 (1.40-1.62), respectively, for patients using CSII versus MDI, the OR was 1.37 (1.34-1.41) and 1.21 (1.17-1.24) for each 1 percentage unit increase in HbA1c, and 2.92 (2.50-3.42) and 2.88 (2.40-3.47) for the care unit with the highest OR versus all other care units.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Probability of having a novel HbA1c check within 4 months after an HbA1c&gt;7%</th>
<th>Probability of having a novel HbA1c check within 7 months after an HbA1c&gt;7%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Univariable</td>
<td>Multivariable</td>
</tr>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>Sex (1=Male; 2=Female)</td>
<td>1.20 (1.12-1.28)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Current age (by 10 years)</td>
<td>0.87 (0.85-0.89)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Diabetes duration (by 10 years)</td>
<td>0.89 (0.87-0.91)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>CSII (0=No; 1=Yes)</td>
<td>1.65 (1.54-1.78)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Current weight (by 10 kg)</td>
<td>0.97 (0.94-1.00)</td>
<td>0.030</td>
</tr>
<tr>
<td>Current BMI (kg/m²)</td>
<td>0.99 (0.98-1.00)</td>
<td>0.039</td>
</tr>
<tr>
<td>Current insulin dose (unit/kg)</td>
<td>0.99 (0.88-1.11)</td>
<td>0.82</td>
</tr>
<tr>
<td>Current calendar year</td>
<td>1.13 (1.11-1.15)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Current HbA1c (% NGS)</td>
<td>1.38 (1.34-1.41)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Unit 1 (0=No; 1=Yes)</td>
<td>0.85 (0.72-1.00)</td>
<td>0.056</td>
</tr>
<tr>
<td>Unit 2 (0=No; 1=Yes)</td>
<td>1.14 (1.00-1.31)</td>
<td>0.052</td>
</tr>
<tr>
<td>Unit 3 (0=No; 1=Yes)</td>
<td>0.80 (0.74-0.87)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Unit 4 (0=No; 1=Yes)</td>
<td>1.63 (1.48-1.80)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Unit 5 (0=No; 1=Yes)</td>
<td>0.56 (0.47-0.65)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Unit 6 (0=No; 1=Yes)</td>
<td>0.83 (0.76-0.92)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Unit 7 (0=No; 1=Yes)</td>
<td>1.17 (1.08-1.26)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Unit 8 (0=No; 1=Yes)</td>
<td>0.79 (0.69-0.90)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Unit 9 (0=No; 1=Yes)</td>
<td>0.91 (0.78-1.06)</td>
<td>0.25</td>
</tr>
</tbody>
</table>
Table 3: Probability of having a novel HbA1c check within 4 months and 7 months respectively after an HbA1c>7 (%), univariable and multivariable GEE model.

| Unit 10 (0=No; 1=Yes) | 2.83 (2.45-3.26) | <.0001 | 2.92 (2.50-3.42) | <.0001 | 2.41 (2.00-2.89) | <.0001 | 2.88 (2.40-3.47) | <.0001 |

Generalized Estimating Equation (GEE) models have been used as they allow for adjustment of within-individual correlation.

Odds-ratio (OR) is describing the effect of the predictor on the outcome variable per 1 unit except for the variables current age, diabetes duration and current weight for which OR is expressing the effect by 10 units.

The OR for a unit is compared is expressing the effect compared to all other units.

Discussion

This retrospective study of 5,989 patients with type 1 diabetes from 10 outpatient diabetes clinics in Sweden during years 2005-2009, shows that annual HbA1c checks were performed less frequently than advocated in clinical guidelines. During the follow-up period, there were 1.75 annual HbA1c checks, on average, during patient periods with HbA1c ≥ 7.0%, while clinical guidelines suggest a check at least every 3rd month after the initial elevated value. In only 35.4% of cases the next HbA1c check following an HbA1c >7% was performed within 4 months. The frequency of annual HbA1c checks was significantly higher for patients treated with CSII compared to MDI, younger individuals compared to older, those with shorter diabetes duration, females, patients with higher HbA1c, and for certain care units. The probability of having an HbA1c check within 4 months after an HbA1c check with a value ≥ 7.0% was approximately 50% greater in individuals treated with CSII compared to MDI. Moreover, the probability of a follow-up HbA1c check at 4 months in patients with inadequate glycaemic control differed between certain care units, with a nearly three-fold increased likelihood among the care unit performing the most annual checks, when compared to the mean number of checks in other care units.

To our knowledge, there is only a single study examining the frequency of HbA1c measurements in patients with type 1 diabetes [20]. In Germany and the UK, electronic medical records were examined from 1,910 and 1,500 patients with type 1 diabetes, respectively, treated in the primary care setting. Patients received, on average, 1.1 annual HbA1c checks in Germany and 2.0 annual checks in the U.K., and investigators concluded that HbA1c checks were underused in both countries. However, we found no previous work examining potential predictors for receiving more frequent annual HbA1c checks in patients with type 1 diabetes, such as those reported here (e.g., CSII and care unit). Recent studies of the frequency of HbA1c measurements in patients with type 2 diabetes or without specifying the type of diabetes, have reported that HbA1c checks are underused in the UK and Australia, without generally examining various predictors for more frequent HbA1c checks [21,22].

One possible explanation for type 1 diabetes patients receiving relatively few HbA1c checks at diabetes care units in Sweden could be a general lack of resources. However, insulin are free, as are glucose monitoring strips, HbA1c tests and insulin pumps if MDI is not used to target good glycaemic control, which is distinguishable from many other countries. Another more likely explanation may therefore be that the number of visits and checks of HbA1c have not been a proper focus of attention in evaluating the quality of diabetes care. In Sweden, the frequency of visits for diabetes care and HbA1c checks are not recorded in the national diabetes registry or in various economic
programs that support care units [13]. Since the mean HbA1c-level during recent years has increased on a national level in patients with type 1 diabetes in Sweden [13], despite increased use of advanced therapies such as CSII, it is possible that there may be problems in the basic care structure for intensive glycaemic therapy. In addition to fewer visits including HbA1c checks, as shown in this study, compliance with regular blood glucose measurements and insulin dosing may also explain these findings.

The number of blood glucose (BG) measurements performed in patients with type 1 diabetes has shown a strong association to the HbA1c-level [23,24]. Good compliance with BG checks has been associated with larger drops in HbA1c than novel therapies such as CSII or insulin analogues [14,23-27]. This may also be reasonable from a clinical perspective since dosage of insulin will not be optimised by bolus correction if BG is not measured before meals. There are yet no studies in Sweden of the general frequency of BG measurements in patients with type 1 diabetes, but our clinical experience is that it is difficult for many patients to comply with BG measurements 4 times per day as advocated in guidelines. One hypothesis is therefore that a reason why HbA1c is not improving in Sweden in spite of patients receiving more modern treatments can be general barriers to adhere to intensive treatment strategies. More frequent clinical visits to diabetes outpatient clinics than the relatively low rate shown here may be essential in supporting patients to comply with BG measurements and insulin dosage, besides other general treatment strategies included in modern diabetes care.

The likelihood of having an HbA1c check within 4 months was approximately 50% greater for patients treated with CSII compared to MDI. It is noteworthy that although if the lower bound of the 95% CI would be true, there was an OR of 1.46 supporting a greater likelihood on treatment. One possible explanation is that patients on CSII need more attention and education to the patient is generally needed.

To improve availability of HbA1c checks, increased resources from care givers may be essential but the responsibility for the individual physician and diabetes educator may also be of concern. Another variable that may have been of interest to evaluate is hypoglycaemia, but this is difficult to record properly in clinical practice for several reasons and the data were judged to be insufficient in the current electronic medical record system. Our finding that more checks were performed in women must be interpreted with caution since it was not possible to exclude periods of pregnancy in all instances, which may result in unknown confounder, although the total time of pregnancy is likely very small compared to all patient years without pregnancy. We did not evaluate explicit visits but the checks of HbA1c per se, but it is noteworthy that in Sweden HbA1c evaluations are in the absolute majority of cases performed in connection to a visit to a physician or diabetes educator.

In conclusion, patients with type 1 diabetes at 10 outpatient diabetes clinics in Sweden had fewer HbA1c checks than advocated in clinical guidelines. More frequent HbA1c checks may improve glycaemic control in the Swedish population. Patients with MDI need to attain extra attention. The frequency of HbA1c checks varies strongly by care unit and needs to be evaluated at the individual diabetes outpatient clinic. Our literature review shows that there previously has been little focus on evaluating the availability of the basic diabetes care in patients with type 1 diabetes. The basic support in diabetes care is probably most crucial in reducing diabetic complications and to give full support to novel therapies to obtain maximal benefit and from a safety perspective.

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Author Disclosure Statement

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