SUMMARY - Forty patients with Type 1 diabetes mellitus were examined on five occasions, three months apart. Their mean (± SD) age was 38.9 (13.2) years. At each visit they participated in a teaching program and also filled out a questionnaire on average morning and daytime blood glucose levels, weekly number of blood glucose measurements and hypoglycaemias. They were then told their last HbA1c value and asked whether they believed the present one would be unchanged (± 0.3 %), slightly higher/lower (0.4-1.0 %), or much higher/lower (more than 1.0 %). They did infrequent home blood glucose monitoring [mean weekly number of measurements 6.9 (6.7)] and did not do systematic self-adjustment of insulin doses. Their HbA1c at inclusion was 9.0 (± 1.6) % and 8.4 (± 1.3) % at the end of the study (p < 0.05). Generally, the changes in HbA1c were few, and only more than 1.0 % in 22.5 % of tests. The kappa values for agreement between predicted and actual HbA1c values at the five visits were between 0.27 and 0.12. The ability to predict HbA1c changes did not improve during the study. A correct prediction (direction of change or no change) was seen in only 45.0 % at the start and 42.5 % at the end of the study. Those predicting correctly did no more home blood glucose measurements than the others. In conclusion, the patients’ own perception of glycaemic control is a poor indicator of HbA1c changes over time.

Key-words: blood glucose control, glycated haemoglobin, Type 1 diabetes mellitus.

RÉSUMÉ - Aptitude des patients diabétiques de type 1 à prédire les changements de leur taux d’HbA1c. Quarante patients diabétiques de type 1 ont été examinés à cinq occasions à trois mois d’intervalle. L’âge moyen était de 38.9 ± 13.2 ans (± DS). A chaque visite ils ont participé à une session d’enseignement et rempli un questionnaire portant sur la moyenne de leurs résultats glycémiques capillaires (au réveil, dans la journée), le nombre de glycémies capillaires pratiquées et d’hypoglycémies hebdomadaires survenues. Ils étaient ensuite informés sur leur précédentes HbA1c et questionnés sur l’évaluation qu’ils faisaient de leur résultat d’HbA1c actuel : inchangée (± 0.3 %), modérément plus élevée ou plus basse (de 0.4 à 1.0 %), ou bien plus haute ou plus basse (plus de 1.0 %). Ils ont pratiqué un faible nombre de mesures capillaires à domicile (6.9 ± 6.7 par semaine) et peu d’auto-ajustement de leur dose d’insuline. Leur HbA1c à l’inclusion était de 9.0 ± 1.6 % et de 8.4 ± 1.3 % en fin d’étude (p < 0.05). En général ce changement d’HbA1c entre les visites était faible et > 1 % chez 22.0 % seulement des patients. La valeur kappa pour la concordance entre HbA1c prédite et mesurée aux 5 visites se situaient entre 0.27 et 0.12. La capacité à prédire l’HbA1c ne s’est pas accrue durant l’étude. Une prédiction satisfaisante (changement et dans quel sens) n’a été notée que chez 45.0 % au début et 42.5 % en fin d’étude. Les patients les plus aptes à prédire leur HbA1c n’étaient ceux pratiquant le plus d’auto-surveillance glycémique. En conclusion, la perception de la qualité de contrôle glycémique par le patient lui-même est un indicateur médiocre du niveau d’HbA1c dans le temps.

Mots-clés: contrôle glycémique, auto-surveillance glycémique hémoglobine glycosylée, diabète type 1.
The Diabetes Control and Complications Trial (DCCT) has made it evident that the level of glycaemic control has a great influence on the development of diabetic long-term complications [1]. Therefore, modern treatment of patients with Type 1 diabetes mellitus aims at normoglycaemia. To achieve this, many Type 1 patients perform numerous blood glucose measurements to make long- or short-term adjustments in their insulin doses. Presumably, these measurements also give the patients a fair idea of whether their glycaemic control is stable, deteriorating or improving.

The measurement of glycated haemoglobin (HbA1c) is another cornerstone in the management of diabetes. The HbA1c value reflects the average blood glucose level during the last six to eight weeks [2], and also correlates well with random blood glucose measurements [3]. Thus, a 1.0 % change in the HbA1c value reflects a change in average blood glucose of approximately 2.5 mmol/L [4, 5], which could be of sufficient magnitude to be recognised by patients if blood glucose is measured frequently. Furthermore, patients with Type 1 diabetes, when informed about changes in their HbA1c levels, often say that the changes were to be expected because of illness, lack of adherence to diet, an observed shift in blood glucose values, or just because of a general feeling. However, whether patients are actually able to predict changes in their HbA1c levels has apparently not been tested before. In the present study the patients were told their last HbA1c value and asked to predict the present one. They were also enrolled in a teaching programme focusing on home blood glucose testing and glycated haemoglobin measurements to see whether the ability to predict changes in HbA1c could be improved.

**PATIENTS AND METHODS**

Patients with Type 1 diabetes mellitus residing in the Tromsø area were recruited if they had a disease duration of more than one year, a good knowledge of their disease and familiarity with home blood glucose testing and the use of multiple injection therapy. They were examined every third month for one year. In each of these five occasions they filled out a questionnaire on average morning and daytime blood glucose, number of weekly blood glucose measurements, hypoglycaemias, and changes in diet and level of physical activity during the last two months. Their answers to the questionnaires were based on memory and not on written notes. They were then told their last HbA1c value and asked whether they believed the present one was approximately the same (± 0.3 %), slightly higher (an increase of 0.4-1.0 %), much higher (an increase of more than 1.0 %), slightly lower (a decrease of 0.4-1.0 %), or much lower (a decrease of more than 1.0 %). For statistical purposes, a prediction was considered correct if it was in the right direction, or if it correctly predicted only a minor change (± 0.3 %). On each occasion they consulted the diabetes nurse individually, and thereafter, in groups of 5 to 10, attended a classroom seminar with a doctor. The seminars focused on the following topics: home blood glucose testing, meaning and importance of glycated haemoglobin measurements, hypoglycaemia, long-term complications, diet, and exercise. HbA1c was analysed by high-performance liquid chromatography (Diamat analyser, Bio-Rad, Richmond, CA; normal range 4.0-6.5 %, coefficient of variation 3.0 %).

The data are presented as the mean (SD). Comparisons between the five visits regarding actual HbA1c values, reported morning and daytime blood glucose values, reported number of blood glucose measurements, and hypoglycaemias, were done using ANOVA with least significant difference (LSD) as post hoc test. For the first visit, linear relations between HbA1c and morning and daytime blood glucose and the number of hypoglycaemias were tested with Pearson’s correlation. The Chi-square test was used to compare the number of correct predictions at the first versus the last visit. As a measure of agreement between the predicted and actual HbA1c levels, the corresponding kappa value was calculated for each visit. In this respect, the predicted and actual HbA1c changes were grouped as “increasing”, “no change”, and “decreasing”. Delta HbA1c (the difference between the present and the last HbA1c value) was calculated for each visit and evaluated in relation to the patients’ predictions, using ANOVA with LSD as post hoc test. The number of blood glucose measurements performed by those having correct and incorrect predictions was compared using Student’s t-test. All tests were performed two-tailed, and p < 0.05 was considered statistically significant. When the same comparison was done at more than one visit, the Bonferroni method for adjusting the p value was used. All statistical analyses were carried out using SPSS version 8.0 software (SPSS Inc., Chicago, IL).

**RESULTS**

Forty-six patients were originally included in the study. Six dropped out after one or two visits, while the rest completed the total program. These 40 patients (26 males) had a mean age (SD) of 38.9 (13.2) years, and mean duration of diabetes was 11.5 (9.4) years. During the study, there was a gradual fall in mean HbA1c (Table I), which at the last visit was significantly lower than at the first (9.0 (1.6) % vs 8.4 (1.3) %, p < 0.05). Reported morning and daytime blood glucose, number of blood glucose measurements, and weekly number of hypoglycaemias remained unchanged throughout the study (Table I).

At the first visit, there was a significant correlation between HbA1c and reported daytime blood glucose (correlation coefficient 0.34, p < 0.05), but not between HbA1c and reported morning blood glucose (correlation coefficient 0.174, p = NS), nor between HbA1c and the number of hypoglycaemias (correlation coefficient - 0.07, p = NS).

Generally, the changes in HbA1c between visits were small, being within ± 0.3 % in 38.5 % of tests, and more than 1.0 % in only 22.0 %. Similarly, patients also expected changes to be within ± 0.3 % in 43.0 % of the tests, and more than 1 % in only 6.5 %.
The number of correct predictions at the first and the last visit did not differ significantly (45.0 % vs 42.5 % respectively) (Table II). The kappa value for agreement between predicted and actual HbA1c levels for the five visits was 0.126, 0.219, 0.268, 0.147 and 0.115 respectively. After correction for repeated measures, none of these values were statistically significant. Delta HbA1c (present minus last HbA1c), in relation to what patients predicted, was consequently lower (more negative) for a prediction of a decrease than an increase (Table III). However, this difference only reached statistical significance at the third visit (p < 0.01).

The number of blood glucose measurements per week did not differ significantly between patients making correct and incorrect predictions at any of the visits (Table IV). Changes in physical activity and diet were few and not related to predicted or actual HbA1c changes (data not shown).

### DISCUSSION

This is apparently the first report on the ability of patients with Type 1 diabetes mellitus to predict changes in their HbA1c levels. Although there was a tendency for a reduction in HbA1c when predicted by patients, overall ability to predict changes was not impressive. Thus, a prediction of a change in the correct direction was seen in less than 50 %, and the kappa value of agreement between predicted and actual levels was below 0.3 on all visits. Furthermore, on the 22 occasions when there was an increase in HbA1c of more than 1.0 %, 12 patients assumed that it was unchanged or lower. Similarly, in 23 cases with a decrease of more than 1.0 %, nine predicted no change or an increase. Accordingly, even major changes were difficult to predict.

There could be several reasons for this. Firstly, the HbA1c assay had a variability that could account for changes almost up to 0.3 %. This obviously explains the inability to predict smaller changes, which, as could be expected [6], were the ones most frequently seen. However, it cannot account for the inability to predict the larger changes described above. Secondly, the patients were not instructed to record blood glucose profiles systematically to help in predicting HbA1c changes. On the contrary, the purpose of this study was to see whether patients with Type 1 diabetes would be able to predict these changes, based on the information they normally possess: their own recollection of blood glucose measurements, hypoglycaemias, level of physical activity, adherence to diet, and possibly their general feeling about glycaemic control. Thirdly, home blood glucose measurements, as in this study, are often performed to solve specific problems related to hypo- or hyperglycaemia, and thus poorly indicative of average levels. Despite this, there was a significant association between reported daytime blood glucose and HbA1c values, indicating at least some relation to mean glycaemic level. However, these blood glucose measurements were not good enough to predict the intraindividual changes.

<table>
<thead>
<tr>
<th>Visit</th>
<th>HbA1c</th>
<th>Morning blood glucose</th>
<th>Daytime blood glucose</th>
<th>Blood glucose measurements</th>
<th>Hypoglycaemias</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9.0 (1.6)</td>
<td>7.1 (2.3)</td>
<td>7.8 (2.6)</td>
<td>6.9 (6.9)</td>
<td>2.2 (2.8)</td>
</tr>
<tr>
<td>2</td>
<td>8.7 (1.5)</td>
<td>7.9 (2.7)</td>
<td>8.0 (2.3)</td>
<td>6.6 (5.4)</td>
<td>1.5 (1.2)</td>
</tr>
<tr>
<td>3</td>
<td>8.6 (1.4)</td>
<td>7.6 (2.1)</td>
<td>7.6 (1.9)</td>
<td>7.1 (6.7)</td>
<td>2.2 (2.9)</td>
</tr>
<tr>
<td>4</td>
<td>8.5 (1.4)</td>
<td>7.9 (2.3)</td>
<td>7.5 (1.9)</td>
<td>7.5 (6.8)</td>
<td>1.7 (1.2)</td>
</tr>
<tr>
<td>5</td>
<td>08.4 (1.3)</td>
<td>7.6 (1.9)</td>
<td>7.5 (1.6)</td>
<td>6.4 (5.6)</td>
<td>1.6 (1.2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Visit</th>
<th>Correct</th>
<th>Overestimation</th>
<th>Underestimation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18 (45.0 %)</td>
<td>9 (22.5 %)</td>
<td>13 (32.5 %)</td>
</tr>
<tr>
<td>2</td>
<td>19 (47.5 %)</td>
<td>14 (35.0 %)</td>
<td>7 (17.5 %)</td>
</tr>
<tr>
<td>3</td>
<td>21 (52.5 %)</td>
<td>11 (27.5 %)</td>
<td>8 (20.0 %)</td>
</tr>
<tr>
<td>4</td>
<td>17 (42.5 %)</td>
<td>17 (42.5 %)</td>
<td>6 (15.0 %)</td>
</tr>
<tr>
<td>5</td>
<td>17 (42.5 %)</td>
<td>16 (40.0 %)</td>
<td>7 (17.5 %)</td>
</tr>
</tbody>
</table>

This pattern of home blood glucose testing could also account for the somewhat surprising observation that the ability to predict HbA1c changes was not related to the number of blood glucose measurements performed.

The patients participated in a teaching programme intended to improve their HbA1c levels as well as their ability to predict HbA1c changes. The first goal appeared at least partly successful, with a reduction in HbA1c from 9.0% to 8.4%. However, as a normal control group was not included, it cannot be excluded that the difference was not due to analytical changes over time. On the other hand, the ability to predict changes in HbA1c levels did not improve during the study, as demonstrated by the kappa values which showed no tendency to increase, and by the almost identical percentage of correct answers at all visits. To achieve truly better prediction, frequent and systematic blood glucose profiles would probably be necessary, with predictions based on recorded values. This remains to be demonstrated in future studies.

The present study has several shortcomings. Only 40 patients were included, and it is likely that the trend towards correct predictions would have proved statistically significant if the group had been larger. Furthermore, our patients on average performed only one blood glucose measurement per day. A different result might have been noted in a cohort of patients doing frequent blood glucose monitoring and systematic self-adjustment of insulin doses. In spite of these shortcomings, it seems fair to conclude that, in the present clinical setting, the ability of patients with Type 1 diabetes to predict even large changes in their HbA1c levels is poor, even after a year’s time and repeated opportunities. Therefore, neither patients nor doctors should rely on anything but objective indicators of long-term glycaemic control, such as HbA1c measurement.

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REFERENCES


