The use of information technology for the management of intensive insulin therapy in type 1 diabetes mellitus

Y Boukhors, R Rabasa-Lhoret, H Langelier, M Soultan, A Lacroix, JL Chiasson

SUMMARY
Objective: The purpose of the study was to evaluate the safety of a computer program used by the patient for the adjustment of insulin doses to achieve tight glycemic control in type 1 diabetic subjects on intensive insulin therapy.

Methods: Ten type 1 diabetic patients participated in the study. Using the basal-bolus (UL-Humalog) insulin regimen, they were randomized in a crossover design to 2 intensive treatment periods of 8 weeks each, one with and the other without the assistance of a computer program via the Internet. They measured their capillary blood glucose regularly, and the results were entered on a daily basis into their log-book or in the computer. During intensive treatment with the computer, the software would provide recommendation for insulin dose adjustment according to specific algorithms. When on intensive treatment without computer assistance, they would adjust their own insulin dose according to the same algorithms.

Results: The study subjects followed 89% of the recommendations made by the computer. With the computer, subjects made more insulin dose adjustments (98 versus 50) than without. Intensive treatments with and without computer assistance resulted in a similar improvement of pre-meal/post-prandial capillary blood glucose from 7.6 ± 2.7/9.5 ± 2.5 to 6.7 ± 2.3/8.8 ± 2.5 and 6.7 ± 2.6/9.0 ± 2.6 mmol/L, respectively. Glycated hemoglobin also improved from 7.7 ± 0.9% to 7.2 ± 0.7 and 7.3 ± 0.8%, respectively. The incidence of minor hypoglycemia was similar under both intensive treatments (7.9 ± 4.0 and 7.1 ± 5.0/patient/28 days, respectively). Both treatments increased patient behavior while patient knowledge of their disease was improved only during computer assistance. There was no effect on quality of life. The study subjects greatly appreciated the software and wanted to continue using it.

Conclusions: The study demonstrated that the use of computer software by the patient to adjust insulin doses for intensive insulin therapy is feasible and is not associated with increased adverse events.

Key-words: Type 1 diabetes - Intensive insulin therapy - Computer.

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The DCCT showed unequivocally that intensive treatment reduced the risk of retinopathy, nephropathy and neuropathy by 50% to 75% when compared to conventional treatment [1]. The lower incidence of complications in intensively-treated patients was seen with a median glycated hemoglobin (HbA1c) level of 7.2% (normal = 4% to 6%) compared with 8.9% in conventionally-treated subjects. Improved glycemic control was achieved through an intensive program where patients were put on multiple daily insulin injections (at least 3 per day) or on continuous subcutaneous insulin infusion. Patients measured their capillary blood glucose 4 times a day and were shown to adjust their insulin dose based on the glucose results, diet and exercise. They were seen monthly by the dietitian, the nurse-educator and the physician. Furthermore, the nurse made weekly phone contact to discuss the glyemic results and to help adjust the insulin doses [1]. Thus blood glucose improvement was the result of more physiologic insulin replacement combined with patient self-management of insulin dose adjustment.

A difficult question raised by the DCCT was whether its results are applicable to type 1 diabetic patients in typical diabetes care settings. To achieve self-management of their disease, diabetic patients need to be educated and to use validated algorithms for insulin dose adjustment [2, 3]. However, one of the frequently encountered problems is that, despite good understanding of the algorithms, patients are hesitant to take the responsibility to increase or decrease their insulin dose. Since DCCT resources are not available in daily practice, we need to develop new tools to help patients adjust their own insulin doses.

For that reason, we have developed a computer program that stores the capillary blood glucose results, analyzes the data and makes specific recommendations for the adjustment of insulin doses. A number of computer program prototypes have already been developed for the management of diabetes [4-6]. Most of these, however, have been developed as teaching tools for health professionals and/or for patient’s education [7-12]. Though some have been developed to provide decision support for insulin dosage adjustment, rare are those that have been validated for safety and efficacy [5, 6, 13].

The purpose of the present study was to assess the safety of the computer program in intensive insulin therapy. The safety of such programs is essential since the DCCT trial has shown that intensive treatment was associated with a 3-fold increase in severe hypoglycemia [1]. We also wanted to determine the impact of the program on knowledge, behavior and quality of life, as well as glycemic control.

Research design and methods

Subjects

Ten type 1 diabetic subjects (7 men and 3 women) participated in the study. Inclusion criteria were: C-peptide-negative, type 1 diabetic subjects of more than 1 year duration, on basal-bolus insulin regimen (ultralente-lispro) for more than 1 month, without any severe hypoglycemia in the previous 6 months, a HbA1c below 150% of normal upper limit and a body mass index (BMI) below 30 kg/m². Patients also had to have a home computer and Internet access. Their mean age was 39.3 ± 10.1 years, BMI was 26.0 ± 3.4 kg/m², the duration of diabetes was 13.9 ± 8.3 years, and mean HbA1c was 7.7 ± 0.9%. One subject had mild retinopathy, 1 had microalbuminuria, and 2 had mild peripheral neuropathy. Three had hypertension and 2 had dyslipidemia.

Insulin dose adjustment

All subjects were familiar with carbohydrate counting and with the adjustment of insulin doses according to specific algorithms (Annex 1) [2, 3]. Carbohydrate counting and insulin dose adjustment was revised with all patients before inclusion. The blood glucose target was between 4 and 7 mmol/L for the pre-meal periods and at bedtime, and between 5 and 10 mmol/L 1 hour after meals [14]. Basal insulin was given as ultralente insulin (Humulin® U) at bedtime and was adjusted by 1 to 2 units at a time to achieve fasting plasma glucose between 4 and 7 mmol/L. Pre-meal insulin was given 5-10 minutes before meals as insulin lispro (Humalog®) in U/10 g of carbohydrates (CHO), as described previously [2, 3, 15, 16]. The dose was adjusted by 0.1 to 0.2 U/10 g of CHO to achieve and maintain 1-hour postprandial capillary blood glucose between 5 and 10 mmol/L or the following pre-meal capillary blood glucose between 4-7 mmol/L. Insulin lispro was injected in the abdomen, and ultralente injection was given in the legs or buttocks throughout the study.

Study design

The study subjects were submitted to 2 months of intensive insulin therapy using a computer program accessible via the Internet and 2 months of intensive treatment without computer in a randomized order and crossover design. All subjects had six visits at the research clinic, 2 before randomization approximately 1 month apart and 2 during each intensive treatment, at the end of month 1 and 2. During computer assisted treatment, each patient had access to a personalized chart via the Internet where he or she was asked to enter his or her capillary blood glucose on a daily basis. The computer would then average the last 3 capillary glucose measurements available (but not beyond 7 days) for each period of the day (before meals and at bedtime) or the measurements since the last insulin dose adjustment. It
would then make recommendations for insulin adjustment according to specific algorithms (Annex 1). During treatment without computer assistance, access to the Internet chart was impossible. The patients would enter their capillary glucose measurements in their log-book and would also make adjustments according to the same algorithms. All subjects were required to measure their capillary blood glucose at least 4 times a day throughout the study. They were also asked to measure their capillary glucose if they had symptoms of hypoglycemia or hyperglycemia. All subjects would fill a nutritional diary at the time of food consumption on 3 representative non-consecutive days (2 week days and 1 week end day) twice during each treatment period at the end of each month. They documented all food items, portions and the amount of CHO in all meals and snacks to check the accuracy of carbohydrate counting. They also included their capillary blood glucose measured before and after (1 hour) each meal and at bedtime (before the bedtime snack) as well as the doses of ultralente insulin and insulin lispro. To estimate the incidence of all hypoglycemia, all capillary blood glucose recorded in their log-book throughout the study were used. Fructosamine and HbA1c were measured before randomization. Fructosamine measurement was then repeated at 1 and 2 months of each intensive treatment, and HbA1c at the end of each treatment period.

All subjects were also asked to answer 3 questionnaires before randomization and at the end of each treatment: 1) a questionnaire on their knowledge of the disease and insulin therapy (30 questions); 2) a questionnaire on their behavior concerning the implementation of intensive insulin therapy (30 questions); and 3) a questionnaire on their quality of life (QOL: 36 open and 38 closed questions). All these questionnaires have been developed and validated in a Canadian population [17-19]. Methodology is described in Annex 2 (unpublished data).

The primary objective of the study was to assess the effect of computer assistance on the frequency of hypoglycemia (capillary blood glucose < 3.0). Secondary objectives included the impact of the computer program on: 1) incidence of hyperglycemia (> 10.0 mmol/L); 2) glycemic control assessed by mean capillary blood glucose, fructosamine and HbA1c; 3) change in knowledge, behaviour and quality of life assessed by mean score of the questionnaires; and 4) change in insulin doses (basal, premeal and total).

The protocol was approved by the Ethic Committee and all subjects signed informed consent.

Laboratory analysis

HbA1c was quantified by high pressure liquid chromatography (Roche Tina Quant II; normal range = 4.0-6.0%) using a DCCT certified method [20]. Intra and inter assay variations are below 3.5%. Fructosamine was measured by calorimetric reaction to nitroblue tetrazolium (normal range = 200-270 μmol/L) [21].

Statistical analyses

Statistical analyses were performed using the paired t-test for all variables. The analyses were done using SAS for Windows (version 8.02, Copyright © 2002 by the SAS Institute, Inc., Cary, NC, USA). All data are expressed as means ± SD.

Table I
Reasons for not following computer program recommendations.

<table>
<thead>
<tr>
<th>Reasons</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Could not access computer</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td>Hyperglycemia between 7 and 8 mmol/L</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td>Morning hyperglycemia</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td>Planning exercise</td>
<td>10</td>
<td>16.7</td>
</tr>
<tr>
<td>Hypoglycemia between 4.0 and 3.6 mmol/L</td>
<td>8</td>
<td>13.3</td>
</tr>
<tr>
<td>Hesitant (afraid)</td>
<td>4</td>
<td>6.7</td>
</tr>
<tr>
<td>Morning hypoglycemia</td>
<td>1</td>
<td>1.7</td>
</tr>
<tr>
<td>Error</td>
<td>1</td>
<td>1.7</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>100</td>
</tr>
</tbody>
</table>

Results

All subjects randomized in the protocol completed the study. No carry-over effect was found between the 2 treatment phases of the study. They measured their capillary blood glucose regularly on an average of 3.4 ± 0.5 times a day.

When on the computer program, they followed the recommendations 89.3 ± 9.9% of the time. They did not follow the computer recommendations 10.7 ± 9.9% of the time for specific reasons listed in Table I. Following the computer program recommendations, the basal insulin (ultralente) dose was adjusted 54 times, and the pre-meal insulin (lispro) dose 44 times. When they were on intensive treatment without computer assistance, they made half as many adjustments of insulin doses: basal insulin was adjusted 41 times, and pre-meal insulin, 9 times. The difference in the total number of adjustments as well as in the number of adjustments for insulin lispro was statistically significant at p < 0.001.

Minor hypoglycemia occurred slightly more often during intensive treatment with the computer but did not reach statistical significance (7.9 ± 4.0 versus 7.1 ± 5.0 patient/month). There was only 1 episode of severe hypoglycemia.
during intensive treatment without computer assistance. Hyperglycemia defined as capillary blood glucose over 10 mmol/L before meals or at bedtime tended to be more frequent without the computer, but was not statistically significant (22.8 ± 18.1 versus 20.6 ± 13.5 patient/month).

Intensive treatments with and without the computer resulted in improvement of capillary blood glucose, as illustrated in Figure 1. Pre-meal capillary blood glucose improved from 7.6 ± 2.7 mmol/L before randomization to 6.7 ± 2.3 and 6.7 ± 2.6 mmol/L after 2 months of intensive insulin therapy with and without computer assistance (p < 0.05). Similarly, post-prandial blood glucose improved from 9.5 ± 2.5 to 8.8 ± 2.5 and 9.0 ± 2.6 mmol/L respectively (p < 0.05) (Fig 1). Metabolic improvement was also confirmed by decreases in HbA₁c from 7.7 ± 0.9% to 7.2 ± 0.7% and 7.3 ± 0.8% respectively (p < 0.05) (Tab II) and lowering of fructosamine levels from 337 ± 41 μmol/L to 310 ± 42 and 313 ± 45 μmol/L at the end of each treatment with and without computer respectively (p < 0.05) (Tab II).

The total daily insulin dose of 66 ± 28 U before randomization did not change significantly with the implementation of intensive insulin therapy whether with or without computer assistance (66 ± 31 and 68 ± 30 U/24 h respectively) (Tab III). However, ultralente tended to increase from 40 ± 18 U to 43 ± 19 and 43 ± 19 U with and without computer assistance respectively (Tab III), while insulin lispro tended to decrease from 26 ± 12 U to 23 ± 14 and 25 ± 14 U, respectively (Tab III). The percentage of basal insulin rose from 60.7 ± 8.4% to 66.6 ± 10.2% and 64.6 ± 11.9% and that of pre-meal insulin declined from 39.3 ± 6.1 to 33.4 ± 10.1 and 35.4 ± 30.2% with or without computer respectively (Tab III).

Table IV details the results of the questionnaires on knowledge, behavior and quality of life. The implementa-

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**Table II**
The effects of intensive insulin therapy with and without computer assistance on HbA₁c and fructosamine.

<table>
<thead>
<tr>
<th>Before randomization</th>
<th>With computer assistance</th>
<th>Without computer assistance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 month</td>
<td>2 months</td>
</tr>
<tr>
<td>HbA₁c (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.7 ± 0.9</td>
<td>7.2 ± 0.7*</td>
<td>7.3 ± 0.8*</td>
</tr>
<tr>
<td>Fructosamine (μmol/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>337 ± 41</td>
<td>318 ± 44</td>
<td>310 ± 42*</td>
</tr>
</tbody>
</table>

*p < 0.05 versus baseline.

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Figure 1
The effects of intensive insulin therapy with and without computer assistance on pre-meal (AC) and post-prandial (PC) capillary blood glucose. The data are means ± SD; *p < 0.05 versus before randomization.
tion of intensive insulin therapy was associated with a significant increase in patient knowledge on the treatment of diabetes when they were on the computer. Similarly, there was a significant increase in their behavior whether they were using the computer or not. However, no change in their quality of life was discernible. Their degree of satisfaction with computer program was quite high (4.2 ± 0.6 on a scale of 1 (low) to 5 (high)). They all wanted to remain on computer assistance and estimated the time required to enter data on Internet chart to less than 5 minutes per day.

Discussion

The present study was designed to test the safety of the use of a computer program by the patient to adjust their insulin doses to achieve and maintain near normoglycemia in the context of intensive insulin therapy in type 1 diabetes. The data show that use of the computer program had no serious adverse effects, can improve knowledge on the disease and was highly appreciated by the study subjects.

Patients were very compliant in measuring their capillary blood glucose (3.4 ± 0.5/patient/day) and entering the results in their log-book and in the computer. While on the computer program, they made 49.7 ± 2.8 entries over 8 weeks for an average of 0.9 ± 0.05 entry per day per subject. Furthermore, they followed the recommendations made by the computer 89% of the time. Moreover, in majority of the cases when computer recommendation was not followed, patients provided rational explanation (e.g. planning exercise). This should be largely sufficient to evaluate the safety of the use of computer program for implementing intensive insulin therapy.

Despite the fact that the subjects were already in relatively good metabolic control at entry into the study, intensive treatments with and without computer assistance resulted in further improvement of pre-meal and post-prandial plasma glucose (Fig 1). In fact, the mean capillary blood glucose levels achieved were well within the recommended target range for optimal control [14]. This was also supported by a parallel improvement in HbA1c and fructosamine (Tab II). The mean HbA1c level achieved (7.2%) was identical to that obtained in the intensive treatment group of the DCCT [1]. We did not observe any significant difference between the 2 intensive treatments whether they used the computer or not, but that was not the objective of the study. We wanted to show that the program was safe and could help the patients to make decisions in the implementation of algorithms to adjust the insulin doses. All study subjects were familiar with the algorithms for insulin dose adjustment. During the last 4 weeks of intensive treatment with the computer, each subject made an average of 9.8 insulin dose adjustments compared to 5.0 without the computer. Since they followed 89% of the recommendations made by the computer, we can conclude that the computer program was safe and helped patients to take decisions.

Only 1 episode of severe hypoglycemia was observed during the study under intensive treatment without computer. The number of minor hypoglycemic episodes was similar under treatment with and without computer assistance (7.9 versus 7.1 per patient/28 days; p = NS). This is similar to that reported in other studies despite the fact that lower HbA1c was achieved in the present investigation [22-24], indicating that the use of a computer program for the adjustment of insulin doses does not result in an increased

Table III
The effects of intensive insulin therapy with or without computer assistance on insulin requirement.

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Before randomization</th>
<th>With computer assistance</th>
<th>Without computer assistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total dose (U/24 h)</td>
<td>66 ± 28</td>
<td>66 ± 31</td>
<td>68 ± 30</td>
</tr>
<tr>
<td>Ultralente [U/day (%)]</td>
<td>40 ± 18 (60.7 ± 8.4)</td>
<td>43 ± 19 (66.6 ± 10.2)</td>
<td>43 ± 19 (64.6 ± 11.9)</td>
</tr>
<tr>
<td>Lispro [U/day (%)]</td>
<td>26 ± 12 (39.3 ± 6.1)</td>
<td>23 ± 14 (33.4 ± 10.1)</td>
<td>25 ± 14 (35.4 ± 30.2)</td>
</tr>
</tbody>
</table>

Table IV
The effects of intensive insulin therapy with or without computer assistance on knowledge, behavior and quality of life.

<table>
<thead>
<tr>
<th>Questionnaires</th>
<th>Before randomization</th>
<th>With computer assistance</th>
<th>Without computer assistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knowledge</td>
<td>82.5 ± 8.4</td>
<td>90.6 ± 6.6**</td>
<td>86.7 ± 7.2</td>
</tr>
<tr>
<td>Behavior</td>
<td>67.8 ± 11.7</td>
<td>74.2 ± 7.8**</td>
<td>73.0 ± 8.5**</td>
</tr>
<tr>
<td>Quality of life</td>
<td>71.2 ± 6.8</td>
<td>72.8 ± 6.1</td>
<td>71.2 ± 9.9</td>
</tr>
</tbody>
</table>

*Score based on 100 points; ** p < 0.01 versus baseline.
risk of hypoglycemia, the most feared adverse event of intensive insulin therapy. The absence of increased incidence in hypoglycemia despite a 50% increase in insulin dose adjustment (98 versus 50 dose modification) confirms the safety of the computer program.

Insulin adjustments with the computer involved nearly equally both basal (55%) and pre-meal insulin (45%). Without the computer, most of the adjustments were with basal insulin (82%), and there were fewer modifications of pre-meal insulin (18%). Despite the significant improvement in glycemic control with the computer, overall daily insulin requirement did not change (66 U/day) (Tab III). However, there was a tendency to redistribute basal and pre-meal insulins; the percentage of ultralente insulin dose increased from 60.7 to 66.6%, while the insulin lispro dose decreased from 39.3 to 33.4%. The changes without the computer were slightly less (64.6 and 35.4% for basal and pre-meal insulin, respectively) (Tab III). This would be consistent with the larger decrease observed in pre-meal capillary blood glucose compared to post-prandial blood glucose (Fig 1). The higher basal insulin dose compared to pre-meal insulin was different from our earlier observations when we were using regular as pre-meal insulin [2, 3, 25]. It is consistent, however, with some [22, 26], but not all [24], of the more recent studies where insulin lispro was given as pre-meal insulin. The differences may be due, at least in part, to the aggressiveness with which morning hyperglycemia was treated. Though their was no systematic blood glucose control at night, this more aggressive treatment of morning hyperglycemia did not result in an increase in overnight reported hypoglycemia.

Implementing this system through Internet can be seen as a limitation. However such a program could also be easily incorporated in a small hand computer including a glucose meter allowing large diffusion and easy access. Such a program can also be customized to treatment regimen and different languages.

High initial scores of knowledge and behavior before randomization show that the patients were already well educated. Intensive insulin therapy with or without computer assistance was associated with an increased behavior while only computer was associated with an increase in knowledge (Tab IV). No change was found in the general quality of life questionnaire scores (Tab IV). Nevertheless, the computer program was considered as a helpful tool by the patients in the implementation of intensive insulin therapy. The significant increase in knowledge with computer assistance is in accordance with the transtheoretical model of change (TMM) of Prochaska which has already been implemented through computerized system in the field of diabetes [27]. According to this model pathways to changes which provides self-care modification posits that patients pass through 5 specific stages (pre-contemplation, contemplation, preparation, action and maintenance) leading to change in health behaviours. It has already been shown that individualised interactive interaction based on TMM constructs are more effective than traditional education approaches [28]. Thus an individualised computer program could help patients to get more rapidly to the action and maintenance stage in the implementation of intensive insulin therapy.

The present study demonstrates that the use of a computer program in the management of insulin adjustment in intensive insulin therapy for type 1 diabetic subjects is feasible, safe and help patients to take decisions. Furthermore, it is highly appreciated by patients. We believe that such a tool could be useful in the long-term glycemic control of type 1 diabetic patients and thus in the prevention of long-term complications. This should be tested in a large population of poorly controlled type 1 diabetic subjects for a longer period of time.

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References

Annex 1
Algorithms for intensive insulin therapy using information technology

1. Target blood glucose
Target blood glucose is between 4 and 7 mmol/L before meal, between 5 and 10 mmol/L after meal. However, for some patients, because of risk of severe hypoglycemia, it may be warranted to increase the targeted blood glucose. A blood glucose below 4 mmol/L at any time is considered hypoglycemia and above 7 mmol/L before meal at bedtime or during the night is considered hyperglycemia.

2. Relevant blood glucose
A blood glucose is said to be “relevant” if it is used to calculate the mean blood glucose to adjust the insulin dose. All blood glucose since the last insulin dose adjustment, which is not associated with a situation that is punctual and exceptional is a “relevant” blood glucose. A blood glucose, however, is said to be “non relevant” if it is associated with a situation that punctual (limited in time) and exceptional (unusual). Finally, a blood glucose is “unusable” if it has already been used in a decision making to adjust the insulin dose.

2.1 Situations that are punctual and exceptional
An hypoglycemia is said to be “non relevant” if it is associated with a situation that is punctual and exceptional such as:
- Unusual physical activities (sports, physical work, shopping, etc.)
- Overestimation of the last insulin dose or having added extra insulin
- Having eaten less than planned for the amount of insulin injected
- Skipped or delayed a meal or snack without modifying the insulin dose
- Unusual alcohol intake within the last 16 hours
- Error (overestimation) in calculating the amount of carbohydrates in the last meal
- Error (overestimation) in calculating the last insulin dose
An hyperglycemia is “non relevant” if associated with a situation that is punctual and exceptional such as:
- Minor illnesses (cold, gastroenteritis, etc.) of less than 3 days
- Intake of more than 15 g of carbohydrate to correct a hypoglycemia
- Stressful situation (limited in time) in the hours preceding the measurement of blood glucose
- Error (underestimation) in calculating the amount of carbohydrates in the last meal
- Error (underestimation) in calculating the insulin dose
- Snack taken before measuring blood glucose

3. Adjusting the insulin dose
A situation of hypoglycemia requires that the dose of the insulin responsible be decreased. A situation of hyperglycemia requires an increase in the dose of insulin responsible. Insulin dose adjustment is based on the mean of the last 2 or 3 measurements of “relevant” blood glucose in each period of the day (before meals and before bedtime), but must not go beyond 7 days.

3.1 There is a situation of hypoglycemia if:
- The mean blood glucose (BG) is below 4 mmol/L.
- The mean BG is equal to or above 4 mmol/L but:
  - There are 2 consecutive “relevant” hypoglycemia (< 4 mmol/L) in one of the period.
  - There are 2 “relevant” non consecutive hypoglycemia before breakfast.
  - There are 3 “relevant” non consecutive hypoglycemia during the last 7 days in one given period.
  - Fasting blood glucose varies more than 10 mmol/L from one day to the next without explanation; under these conditions, it will be recommended to measure the BG during 2 consecutive nights, and if one is < 4 mmol/L, it will be considered as a situation of hypoglycemia.

3.2 There is a situation of hyperglycemia if:
- The mean of the last 2 or 3 blood glucose is above 7 mmol/L. However, the recommendation to increase the insulin dose will be put on hold if:
  - Only one of the last 3 BG is > 7 mmol/L.
  - One of the last 3 BG is < 4 mmol/L.
  - The fasting BG differ by more than 10 mmol/L between 2 consecutive BG measurements; under these circumstances, it will be recommended to measure BG during 2 consecutive nights and if one is < 4 mmol/L it will be considered as a situation of hypoglycemia.

3.3 Which insulin should be adjusted?
- Always check to see if:
  - The basal insulin (Ultralente) was adjusted in the last 3 days; or
  - The pre-prandial insulin (Humalog®) over the last 2 days.
Under these 2 conditions, it is called a “waiting period” and no insulin adjustment must be made. One exception, however – if there are 2 consecutive relevant hypoglycemia in the morning, then the ultralente should be decreased.
Therefore, if there is a situation of hypoglycemia or hyperglycemia:
• During the night or before breakfast – the dose of ultralente must be adjusted;
• Before meal or at bedtime, the dose of Humalog® for the preceding meal must be adjusted.

The dose ultralente will be changed by:
• 1 unit of the total dose is < 10 U
• 2 units if the total dose is ≥ 10 U

The dose of Humalog® will be changed by:
• 0.1 U/10 g CHO if the dose per 10 g of CHO is < 1.0 U
• 0.2 U/10 g CHO if the dose per 10 g of CHO is ≥ 1.0 U

Annex 2
Quality of life questionnaire validation

The quality of life questionnaire that we have used in this study was validated in both French (n = 300) and English (n = 300) Canadian subjects, in diabetic (n = 150) as well as non diabetic (n = 150) subjects.

We first created an open-ended questionnaire covering all the dimensions affecting quality of life: physical and psychological well-being, social and family life, religion, finances, work, scholarship, and recreation. This questionnaire was administered to men and women (50/50) of different ages (20 to 70 years and up), to type 1 and type 2 diabetics, as well as non diabetics. The diabetic subjects were selected in sequential order according to their presentation at the out-patient clinic at the Hôtel-Dieu Hospital in Montreal and at the Foothill’s Hospital in Calgary. The non diabetic subjects were paired with the diabetic subjects according to age, sex, and residential area. They were recruited using the “random digit dialing technique”.

This first questionnaire allowed us to identify the most important problems affecting the quality of life of diabetic subjects. Based on this information, we formulated a final instrument to measure the quality of life in the form of a close-ended questionnaire. This final instrument was validated in both French and English, as well as in diabetic and non diabetic subjects, by testing for comprehension (non ambiguity) of the questions, the reproducibility, and the sensitivity. Among the original subjects who participated in the open-ended questionnaire, 120 participated in the comprehension validation; every question that had to be corrected underwent a second evaluation. Forty diabetic subjects participated in the reproducibility validation. These subjects were relatively stable in their psychological and physical health while they were submitted to 2 questionnaires 2 months apart. The good correlation between the first and second interview confirmed the good reproducibility. Another 40 diabetics participated in validating the sensitivity of the questionnaire. These patients had to be put on insulin therapy because of poor glycemic control. They were interviewed before and 2 months after intervention. A good correlation was established between the improvement of their glycemic control and the improvement in their senses of well being indicating a good sensitivity of the instrument. The questionnaire was also administered twice to 90 non diabetic subjects at 2-month interval. Those who reported major events according to the Sarason’s stress test during the last 2 months were used for sensitivity evaluation and others for reproducibility. The instrument was found to be reproducible and sensitive in the non diabetic population as well as in the diabetic population.