Original article

Basal insulin dose in 40 type 1 diabetic patients remains stable 1 year after educational training in flexible insulin therapy


Department of Endocrinology, Pôle DigiDune, Grenoble University Hospital, Joseph-Fourier University, BP 217X, 38043 Grenoble, France

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Abstract

Aim. – Basal insulin dose (BID) determination is the key to successful flexible insulin therapy (FIT). As our hypothesis was that BID changes over time, the primary objective of the present study was to determine the changes in BID 1 year after a therapeutic educational programme on FIT.

Methods. – This single-centre retrospective study recruited the first 40 type 1 adult diabetic patients undergoing an educational FIT programme, which was conducted over a 4-day hospital stay and included a carbohydrate-fasting test.

Results. – Patients’ BIDs decreased between Day 0 and Day 4 after the programme (0.31 ± 0.11 IU/kg/day vs 0.27 ± 0.09 IU/kg/day; P < 0.0001), and was increased at 1 year (0.29 ± 0.09 IU/kg/day; P = 0.004). There was no significant variation in prandial insulin requirements. A tendency toward a reduction in HbA1c was observed at 1 year (8.3 ± 1.4% vs 8.1 ± 1.6%; P = 0.075), with a decrease by more than 0.5% in 37.5% of patients. Body weight increased at 1 year (66.9 ± 10.4 kg vs 68.1 ± 10.7 kg; P = 0.003), and the gain was greater than 5% in 7.5% of patients. Frequency of mild hypoglycaemia either remained stable (40%) or decreased (30%). Only nine patients (baseline HbA1c 8.03 ± 1.7%, baseline BID 0.27 ± 0.09 IU/kg/day) had BID increases more than 20%, with no changes in prandial insulin requirements and no distinctive phenotype. Baseline HbA1c, and BID have an impact on the BID at 1 year of approximately 0.3 IU/kg/day in most patients.

Conclusion. – The stability of BID over 1 year, with values close to 0.3 IU/kg/day associated with a trend towards improvement in HbA1c, reduction in the frequency of mild hypoglycaemic episodes and absence of major weight gain, supports the relevance of FIT educational training.

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Keywords: Flexible insulin therapy; Therapeutic education; Type 1 diabetes; Basal insulin

Résumé

La dose d’insuline basale déterminée chez 40 diabétiques de type 1 par une éducation thérapeutique à l’insulinothérapie fonctionnelle demeure stable à un an.

Contexte. – La détermination des doses d’insuline basale (DIB) est un élément clé du succès d’une approche d’insulinothérapie fonctionnelle (IF). Notre hypothèse était que les DIB dérivent dans le temps. Notre objectif était de déterminer l’évolution des DIB un an après éducation thérapeutique à l’IF.

Méthodes. – Étude rétrospective monocentrique réalisée chez les 40 premiers patients diabétiques de type 1 adultes qui avaient bénéficié d’un programme d’éducation à l’IF, réalisé au cours d’une hospitalisation de quatre jours avec épreuve de jeûne glucidique.

Résultats. – Les DIB ont diminué entre j0 et j4 après stage (0.31 ± 0.11 vs 0.27 ± 0.09 UI/kg par jour, P < 0.0001) puis augmenté à un an (0.29 ± 0.09 UI/kg par jour, P = 0.004). Il n’y avait pas de variation des besoins en insuline prandiale. Une tendance à une diminution de l’HbA1c a été observée à un an (8.3 ± 1.4 vs 8.1 ± 1.6%, P = 0.075), avec une réduction de plus de 0.5% chez 37,5% des patients. Le poids a augmenté (66.9 ± 10.4 vs 68.1 ± 10.7 kg, P = 0.003), de plus de 5% chez 7,5% des patients. La fréquence d’hypoglycémies modérées est restée stable (40%) ou a diminué (30%). Seuls neuf patients (HbA1c initiale 8.03 ± 1.7%, DIB 0.27 ± 0.09 UI/kg par jour) ont augmenté leur DIB de plus de 20%, sans variation des besoins en insuline prandiale, ni phénotype distinct. L’HbA1c et la DIB initiales influencent l’évolution de la DIB à un an, convergeant vers 0.3 UI/kg par jour chez la majorité des patients.

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Keywords: Flexible insulin therapy; Therapeutic education; Type 1 diabetes; Basal insulin
**1. Introduction**

Intensive insulin therapy, involving basal insulin administration to control fasting and prandial blood glucose levels, and bolus insulin administration to control postprandial blood glucose peaks, is the gold standard of treatment for type 1 diabetes patients [1]. For years, patients have been instructed to follow a strict dietary plan with predetermined, stable carbohydrate intakes. However, flexible insulin therapy (FIT) is now being recommended more frequently, thus allowing greater dietary freedom, provided that the patient has been taught how to estimate carbohydrate intakes and how to determine the corresponding rapid-acting insulin dose requirements [2–5].

In addition to improving quality of life, FIT allows for improved glycaemic control without increasing the occurrence of hypoglycaemia and, in particular, severe hypoglycaemic episodes [2–4]. The fact that hypoglycaemic episodes are not more common following FIT may be attributed to the precise assessment of basal insulin requirements regardless of the method used (calculation based on weight, carbohydrate-fasting tests or a complete fast).

Although the precise definition of FIT is still a matter of debate, it is well established that the precise determination of the basal insulin dose (BID) ensures the success of this therapeutic approach. In practice, however, the routine assessment of glycaemic control relies on prandial values, which are more commonly available than postprandial values. This strategy tempts both the patient and physician to increase BID should there be inadequate control of prandial blood glucose levels. Therefore, our working hypothesis was that, following an educational FIT training programme, patients would be inclined to increase their BID over time, thereby overestimating their basal insulin/prandial insulin ratio. This would reduce glycaemic control, resulting in both early postprandial hyperglycaemia and late postprandial hypoglycaemia.

The primary objective of the present study was to determine changes in BID 1 year after an FIT training programme. The secondary objective was to account for potential BID anomalies based on the clinimetrics used in diabetology.

**2. Methods**

This single-centre retrospective study focused on the Grenoble University Hospital’s FIT educational programme for adult diabetics. The training was carried out in groups of six patients during a 4-day hospital stay under the management of a diabetologist, a dietitian and a nurse, and included a carbohydrate fast undertaken on the first day to determine BID.

The effectiveness of the training programme was evaluated 3 months later during a follow-up patient’s consultation. The inclusion period started in March 2003—when the programme began—and ended in December 2005, which meant that all recruited patients had a follow-up period of at least 12 months. All consecutive type 1 diabetic patients who received the train-
Table 1
Patients’ clinical characteristics according to type of insulin treatment.

<table>
<thead>
<tr>
<th></th>
<th>Total population (n = 40)</th>
<th>Patients taking glargine (n = 29)</th>
<th>Patients using insulin pump (n = 10)</th>
<th>Patients using NPH insulin (n = 1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (range)</td>
<td>36.2 ± 14.5 (13–70)</td>
<td>37.1 ± 15 (16–70)</td>
<td>35.0 ± 14.1 (13–55)</td>
<td>26</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>18/22</td>
<td>13/16</td>
<td>5/5</td>
<td>Female</td>
</tr>
<tr>
<td>Diabetes duration (years) (range)</td>
<td>14.3 ± 10.4 (0–43)</td>
<td>13.4 ± 9.1 (0–39)</td>
<td>16.9 ± 14.4 (2–43)</td>
<td>17</td>
</tr>
<tr>
<td>Duration of basal-bolus treatment (years)</td>
<td>1.2 ± 1.9</td>
<td>0.8 ± 0.9</td>
<td>2.5 ± 3.2</td>
<td>NA</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>66.9 ± 10.4</td>
<td>67.5 ± 10.3</td>
<td>65.7 ± 11.3</td>
<td>59</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23.3 ± 3.1</td>
<td>23.0 ± 2.9</td>
<td>24.1 ± 3.9</td>
<td>22.2</td>
</tr>
<tr>
<td>HbA1c (%) (range)</td>
<td>8.3 ± 1.4 (5.6–12.8)</td>
<td>8.5 ± 1.6 (5.6–12.8)</td>
<td>7.9 ± 0.7 (6.9–9.6)</td>
<td>7.7</td>
</tr>
<tr>
<td>Basal/weight (IU/kg/day)</td>
<td>0.31 ± 0.11</td>
<td>0.30 ± 0.08</td>
<td>0.34 ± 0.17</td>
<td>0.47</td>
</tr>
</tbody>
</table>

Data are expressed as means ± standard deviation; NA: not applicable.

Table 2
Changes 1 year after patients’ training in flexible insulin therapy in basal insulin doses (BIDs), HbA1c, weight, frequency of mild hypoglycaemic episodes and frequency of blood glucose self-monitoring.

<table>
<thead>
<tr>
<th></th>
<th>Increased [n (%)]</th>
<th>Stable [n (%)]</th>
<th>Decreased [n (%)]</th>
<th>Total [n (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIDs (±20%)</td>
<td>9 (23.1)</td>
<td>28 (71.8)</td>
<td>2 (5.1)</td>
<td>39 (100)</td>
</tr>
<tr>
<td>HbA1c (±0.5%)</td>
<td>5 (12.8)</td>
<td>19 (48.7)</td>
<td>15 (38.5)</td>
<td>39 (100)</td>
</tr>
<tr>
<td>Weight (±5%)</td>
<td>8 (20)</td>
<td>32 (80)</td>
<td>0 (0)</td>
<td>40 (100)</td>
</tr>
<tr>
<td>Mild hypoglycaemia</td>
<td>6 (16.2)</td>
<td>19 (51.3)</td>
<td>12 (32.4)</td>
<td>37 (100)</td>
</tr>
<tr>
<td>Frequency of blood glucose self-monitoring</td>
<td>6 (15)</td>
<td>29 (72.5)</td>
<td>5 (12.5)</td>
<td>40 (100)</td>
</tr>
</tbody>
</table>

3. Results

3.1. Baseline patients’ characteristics

In total, 48 type 1 diabetic patients attended the training programme, of whom eight were excluded due to changes in basal insulin within the first year (initial HbA1c 7.7 ± 0.7%, baseline BID 0.43 ± 0.33 IU/kg/day). Thus, the present study included 40 patients, whose baseline characteristics are summarized in Table 1. Patients’ mean ± standard deviation (SD) age was 36.2 ± 14.5 years, diabetes duration was 14.3 ± 10.4 years and HbA1c was 8.3 ± 1.4%. One patient was still being treated with neutral protamine Hagedorn (NPH) insulin, as patient recruitment began in 2003, when insulin glargine first came onto the market in France. Patients’ characteristics did not significantly differ with the different types of basal insulin therapy. The baseline BID of the whole study population was 0.31 ± 0.11 IU/kg/day.

3.2. Overall changes at 1 year

Overall results at the 1-year follow-up are summarized in Table 2. However, 1-year data were not available for all patients. BID remained stable in 71.8% (28 out of 39 patients), increased in 23.1% (nine out of 39 patients) and decreased in 5.1% (two out of 39 patients), while HbA1c remained stable in 48.7% (19 out of 39 patients), decreased in 38.5% (15 out of 39 patients) and increased in 12.8% (five out of 39 patients). Weight remained stable in 80% (32 out of 40 patients), and increased in 20% (eight out of 40 patients). The incidence of non-severe hypoglycaemic episodes remained unchanged in 51.3% (19 out of 37 patients), decreased in 32.4% (12 out of 37 patients) and increased in 16.2% (six out of 37 patients). As for behaviour at 1 year, 75% of patients continued to count carbohydrates to assess their prandial insulin requirements, and 66% were injecting extraprandial insulin correction doses. Compliance with blood glucose self-monitoring remained stable in 72.5% (29 out of 40 patients), and increased in 15% (six out of 40 patients). At 1 year, blood glucose was monitored at least five times a day in 77.5% of patients.
3.3. Basal insulin dose changes

Details of the changes in insulin doses are shown in Fig. 1. Although BID was significantly reduced during the training program (0.31 ± 0.11 IU/kg/day vs 0.27 ± 0.09 IU/kg/day; \( P < 0.0001 \)), significant BID re-escalation was observed at 1 year, albeit without reaching baseline levels (0.27 ± 0.09 IU/kg/day vs 0.29 ± 0.09 IU/kg/day; \( P = 0.004 \)). It is also worth noting that, in this retrospective study, no significant difference was observed between BID at 3 months (collected from patients’ files at a compulsory assessment visit) and at 12 months (collected from patients’ files or self-reported; Fig. 1). Excluding a subgroup of nine patients whose BID increased by more than 20%, BID remained stable throughout the year following the training course in the 30 remaining patients (Fig. 2). In two out of 39 patients, BID was reduced by more than 20% whereas, in 28 out of 39 patients, BID was within the ±20% interval and, in eight patients, remained unchanged.

The phenotype (weight, HbA1c, diabetes duration and BID) and behaviour (self-monitoring and follow-up) of the nine patients whose BID increased by more than 20% did not differ significantly from that of the other patients. However, this subgroup tended to be younger [31.4 ± 12.5 years vs 37.7 ± 14.9 years; not significant (ns)], and had shorter diabetes duration (10.1 ± 8.2 years vs 15.6 ± 10.8 years; ns) and a lower baseline BID (0.27 ± 0.09 IU/kg/day vs 0.33 ± 0.11 IU/kg/day; ns). Also, baseline HbA1c in these nine patients exceeded 8% (8.03 ± 1.68% and was not significantly reduced 1 year after the programme (7.73 ± 0.84%; ns). In addition, at 1 year, BID no longer differed between the two study populations (0.30 ± 0.12 IU/kg/day vs 0.29 ± 0.09 IU/kg/day; ns; Fig. 2).

Prandial insulin doses (PIDs) did not change significantly over time (data not shown). Although a potential anomaly resulting in basal insulin covering part of the prandial insulin requirements was sought, no such anomaly was found. In the 30 patients with stable or reduced BID, the BID was identical to their PID prior to the fasting test (BID/PID = 1.02). However, this ratio decreased after the carbohydrate-fasting test (BID/PID = 0.88; \( P = 0.26 \)), but increased again at 1 year (BID/PID = 0.97; \( P = 0.43 \)). Nevertheless, these variations were not significant, and the ratio remained less or equal to 1. Similar results were seen in the nine patients whose BID increased by more than 20%. Furthermore, treatment type (insulin pump vs glargine) had no impact on BID changes (data not shown).

Baseline HbA1c appeared to influence BID changes at 1 year (Table 3). Patients with baseline HbA1c less than 7% (\( n = 8 \)) between 7–8% (\( n = 13 \)) and greater or equal to 8% all showed initial significant decreases in BID after the fasting test. Later, both the less than 7% and 7–8% groups had stable BIDs, whereas the greater or equal to 8% group showed a moderate increase in BID at 1 year, with a statistically significant difference compared with baseline. Interestingly, the less than 7% group had the lowest BID at the end of carbohydrate-fasting, which was still present at 1 year (0.21 ± 0.11 IU/kg/day) compared with the 7–8% (0.29 ± 0.09 IU/kg/day; ns) and greater or equal to 8% (0.31 ± 0.08 IU/kg/day; \( P = 0.06 \)) groups.

Baseline BID levels had an influence on future changes (Table 3): patients with baseline BID levels less than 0.3 IU/kg/day continued to have a low BID. In contrast, patients with baseline BID levels greater or equal to 0.3 IU/kg/day—above the theoretical requirements of 0.3–0.4 IU/kg/day—benefited the most from the BID decrease, which began at the end of the fasting test and lasted up to 1 year.

3.4. Progression of other indicators

Overall, a tendency toward a decrease in HbA1c was observed at 1 year (8.3 ± 1.4% vs 8.1 ± 1.6%; \( P = 0.075 \)), with a decrease of more than 0.5% in 37.5% of patients. The nine patients with BID increases of more than 20% also showed a tendency toward an improvement in HbA1c values (8.03 ± 1.68% vs 7.73 ± 0.84%; ns). Patients with the poorest baseline HbA1c (>8%; \( n = 23 \)) showed more marked improvements, although the changes were not statistically significant (9.1 ± 1.0% vs 8.6 ± 1.8%; \( P = 0.06 \)). As for patients with baseline HbA1c values less than 7% (\( n = 5 \)), although their HbA1c levels remained unchanged, they experienced fewer non-severe hypoglycaemic episodes in the year following the training. As for severe hypoglycaemia, 10 patients reported one or two episodes within 12 months of finishing the programme, with no correlation with HbA1c. However, data on the incidence of such episodes prior to the programme was not collected. While weight tended to
moderately decrease at 6 months, it was significantly increased at 1 year (66.9 ± 10.4 kg vs 68.1 ± 10.7 kg; P = 0.003).

4. Discussion

Determining the BID is the key to successful FIT. The present study assessed the effects of a hospital-based training programme at 1 year and revealed three factors.

First and foremost, the study confirmed that basal insulin overdosing is widespread, as has been previously reported by other French researchers [4,6]. The carbohydrate-fasting test, which has both diagnostic and pedagogic value, demonstrated this tendency well. In our patients, the fasting test brought about a significant reduction in BID by an average of approximately 3 IU/day. According to the published data on type 1 diabetic patients, basal insulin requirements range from 0.3 to 0.4 IU/kg/day [10,11]. Other authors have used different algorithms in which basal insulin requirements are estimated to be 50% of daily doses, ranging from 0.5 to 0.7 IU/kg/day. The initial overestimation of BID in our patient population may be accounted for by an inadequate distribution between basal and PIDs. The ratio between BID and PID decreased on completion of the training programme, and stabilized at less than 1 year. Interestingly, the patients with decreased BIDs were those whose baseline BIDs were above the maximum theoretical requirements of 0.4 IU/kg/day, whereas those whose baseline BIDs were already low experienced no significant changes over time.

Another finding of the present study was that the BID determined during the training course was an appropriate measure, as no major adjustments were made to it during the following year. Although BID re-escalation at 1 year achieved statistical significance, the changes did not exceed 20% in the majority of patients, amounting to 1.3 IU/day on average. This is in line with the data reported by other researchers in Switzerland, Quebec and Germany, based on a 3-year follow-up period [7–9]. The persistent BID reduction contributed to a lower incidence of mild hypoglycaemic episodes with no HbA1c deterioration; indeed, the latter parameter was actually improved. The lower risk of hypoglycaemia is in accordance with data from French and Swiss investigators, who reported a decreased frequency of severe hypoglycaemic episodes associated with a decrease in insulin doses among patients who underwent FIT training compared with those who continued with conventional insulin therapy [4,7]. However, the present retrospective study did not quantify the incidence of severe hypoglycaemic episodes prior to the training programme. Nevertheless, in the present study, BID changes did not differ according to type of basal insulin therapy (glargine or pump). Similarly, our pump patients did not have lower BIDs than those using multiple injections, contrary to observations made by others [12–14], although reported BID differences are usually very small when glargine is considered.

A third factor brought to light by our present study was that some patients showed a marked increase in BID—exceeding 20%—as determined by carbohydrate-fasting tests. However, this was a minority subgroup of nine out of 39 patients (23%), characterized by a low BID prior to fasting tests (0.27 IU/kg/day) and HbA1c greater than 8%. At 1 year, this subgroup reached a BID of 0.3 IU/kg/day, in conformity with theoretical requirements. The reason why this population had such a low baseline BID is unclear. It should be borne in mind that, as these patients did not reduce their PIDs, their BIDs remained below prandial dose levels. Basal insulin requirements depend on several parameters: body mass index (BMI), insulin sensitivity, insulin bioavailability, HbA1c, residual insulin secretion and the presence of lipodystrophy [10,11]. It may be speculated that the correction of lipodystrophy zones, which is the subject of specific recommendations in our training course, and the adoption of strict rules, which may decrease over time after the training course, were possibly contributory to the dose escalation.

Finally, it should be noted that the patients with the lowest baseline HbA1c (< 7%) were also those with the lowest BID both following the carbohydrate fast and at the 1-year follow-up, whereas their diabetes duration was not shorter, being around 15 years on average. Also noteworthy is that the patients with a baseline BID far below the theoretical requirements maintained a low BID throughout the study period.

To confirm our data, it would be of interest to develop customized algorithms based on multicentre study results and taking into account the various parameters that influence basal insulin requirements (previous HbA1c, weight, diabetes duration, hypoglycaemic episodes, previous basal and total insulin doses, lipodystrophy). The ultimate goal is to limit the risk of BID anomalies due to either excessive doses, exposing the patient to hypoglycaemic episodes, or underestimated doses, exposing the patient to poor HbA1c control. In this regard, our present study

Table 3
Changes in basal insulin dose (BID) after training in flexible insulin therapy in relation to baseline HbA1c and BID.

<table>
<thead>
<tr>
<th>BID</th>
<th>HbA1c (%)</th>
<th>Day 0 BID (IU/kg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 7</td>
<td>7–8</td>
<td>&gt; 8</td>
</tr>
<tr>
<td>Day 0</td>
<td>0.28 ± 0.14</td>
<td>0.34 ± 0.13</td>
</tr>
<tr>
<td>Day 4</td>
<td>0.20 ± 0.15a</td>
<td>0.28 ± 0.08b</td>
</tr>
<tr>
<td>Day 360</td>
<td>0.21 ± 0.11</td>
<td>0.29 ± 0.09</td>
</tr>
</tbody>
</table>

Data are Mann–Whitney test results expressed as means ± standard deviation.

a P < 0.05, Day 4 vs Day 0.
b P < 0.05, Day 360 vs Day 0.
c P < 0.05, Day 4 vs Day 360.
d P = 0.06, group < 7 vs group > 8.
e P < 0.05, group < 0.3 IU/kg/day vs group > 0.3 IU/kg/day.
findings suggest that such a risk is low in patients undergoing educational FIT training.

In conclusion, FIT training of 48 type 1 diabetes patients resulted in either stabilization (53%) or reduction (36%) of HbA1c while maintaining or reducing BID in 77% of patients, with weight stabilization observed in 79%, stabilization of mild hypoglycaemic episodes in 47% and reduction of mild hypoglycaemic episode frequencies in 34% of patients. BID, determined by carbohydrate-fasting tests, remained stable at close to 0.3 IU/kg/day in the majority of cases, except in a small subgroup of patients whose only specific features were a low baseline BID (< 0.30 IU/kg/day) and high HbA1c (> 8%) levels. These results confirm the relevance of the use of FIT in type 1 diabetic patients.

Conflict of interest statement

The authors declare no conflicts of interest.

References