

Delay in starting insulin after failure of other treatments in patients with type 2 diabetes mellitus

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Abstract

Background and aim: In type 2 diabetes mellitus (T2DM), therapies to maintain blood glucose control usually fail after several years. The aim of this study was to estimate the time to insulin initiation, the glycemic burden that patients are exposed prior to conversion to insulin and their HbA1c level at that time and a year later.

Material and Methods: Five hundred nine patients were included in this retrospective study. We identified patients with T2DM who started insulin therapy from 01/01/2002 to 30/06/2011, from the Scottish Care Information-Diabetes Collaboration (SCI-DC) database of Western General Hospital, Edinburgh, Scotland. We estimated the duration of diabetes prior to conversion to insulin therapy, the months they spent with glycated hemoglobin (HbA1c) above 7%, 8% or 9% until starting insulin, HbA1c and body weight (BW) at the time of conversion, at 6 and at 12 months before and after conversion.

Results: Patients started insulin therapy after a median period of 6.2 (1-30) years after diagnosis of T2DM. Median HbA1c was 10% (range 7.2-17.9) at the time of conversion, 8.8% (5.8-16.9) at six months before and 8.3% (5.2-15) at 12 months before conversion, and 8.4% (4.7-14.3) at 6 months and 8.2% (5-14.7) at 12 months after conversion. Body weight (BW) was 86.6 kg (39.6-179.8) at the time of conversion and 91 kg (42.7-196) at 12 months after conversion. Patients spent a median period of 49 (0-325) months with HbA1c >7%, 25 (0-163) months with HbA1c >8% and 10 (0-135) months with HbA1c >9%. Insulin treatment resulted in a decrease in HbA1c at 12 months of 1.8% ($p < 0.05$) but in an increase in BW by 2.9 kg ($p < 0.05$).

Conclusion: Healthcare professionals delay the initiation of insulin in patients with type 2 diabetes until their HbA1c exceeds 10%. As a result, patients are exposed to a significant glycemic burden. Change in treatment improves their glycemic control for the next 12 months. Hippokratia 2014; 18 (4): 306-309.

Keywords: Diabetes mellitus type 2, insulin therapy, glycemic burden

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Introduction

Diabetes mellitus is a chronic disease associated with macrovascular and microvascular complications¹⁻³. Although it is well known that glycemic control plays a crucial role in preventing these complications^{4,5}, less than half of the patients with diabetes achieve their glycemic target⁶. Moreover, oral antidiabetic drugs (OAD) fail to maintain glucose levels and sooner or later many patients require insulin therapy. An important issue is that healthcare professionals or patients often delay starting insulin and patients are therefore exposed to significant hyperglycemia for a long period of time.

In this study we aimed to evaluate how long it takes from diagnosis, for our patients with type 2 diabetes mellitus (T2DM) to start insulin therapy, how many months they spend with uncontrolled diabetes, meaning months with glycated hemoglobin (HbA1c) above 7%, 8% or 9%, and at what HbA1c level, insulin therapy is commenced when other treatments fail to maintain glycemic control.

Subjects and methods

In this retrospective study, we analysed medical records of patients with T2DM who were converted to insulin therapy from 01/01/2002 to 30/06/2011 at the Metabolic Unit of Western General Hospital, Edinburgh, Scotland. We used the Scottish Care Information-Diabetes Collaboration (SCI-DC) of Western General Hospital to define a cohort of patients with diabetes who were on any insulin therapy over this period. SCI-DC database covers the majority of the Scottish population with diagnosed T2DM, as almost all adult patients are registered on the SCI-DC database since 2000. SCI-DC database contains also retrospective data, uploaded from other electronic healthcare records at the time of the initial entry of a patient onto the database, so we had information regarding our patients before their first visit to the clinic. Data from all patients receiving an insulin prescription during this period and HbA1c, Body Weight (BW) and Body Mass Index (BMI) were extracted from this data-

base. To retrieve the files we used key-words involving all the names of insulin used.

Patients who started insulin in less than 12 months from diagnosis were excluded to avoid undiagnosed type 1 diabetes, as well as patients who were converted to insulin during pregnancy or planning pregnancy, during acute illness other than uncontrolled diabetes or hospitalization. Finally, files with insufficient data, as those having less than 3 visits in our clinic or no information regarding HbA1c and BW before and after conversion, were omitted. Time of conversion was considered the last visit of a patient to our clinic before starting insulin. We retrieved data from that visit regarding HbA1c and BW. For the 6 months information we used any data between 3-9 months before or after conversion and when there were more visits or results, we used those which were closest to the 6 month point. For the 12 months the data was collected between 9-15 months and nearest to the date of the 12 month.

We estimated the time of uncontrolled diabetes by counting the months that a patient had HbA1c above 7%, 8% or 9%. Our patients usually had a repeat HbA1c every 6 months, or sooner if they are not well controlled, so we counted the months from an elevated HbA1c until the next measurement to be below 7% or 8% or 9%. If a patient was lost to follow up for 2 years or more, we excluded this period of time. We finally calculated the time from diagnosis until their conversion to insulin therapy and the time from their initial entry in the SCI-DC database, considering it as their first visit to a health professional [General Practitioner (GP) or Diabetologist (DT)].

Statistical analysis

All data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 13 (SPSS Inc., Chicago, IL, USA). Normality of distribution was assessed by Kolmogorov-Smirnov test. Continuous data are presented as median and range and categorical data as absolute numbers and percentages. Comparisons were performed by paired t test and Wilcoxon Signed rank test for normal and non-normal distributions respectively. In all cases, a 2-tailed p value less than 0.05 was considered statistically significant.

Results

From 11,029 patients with type 2 diabetes, 1,364 had an insulin prescription. From these, 529 had started insulin before 2002, 99 were on insulin from their first visit or started insulin in less than 12 months from diagnosis, 22 were converted during pregnancy or planning pregnancy, 5 proved to have type 1 diabetes, 32 were converted during hospitalization for acute illness and 10 proved not to be on insulin. Finally from 1,221 files with sufficient data, 509 fulfilled the inclusion criteria.

Median age of the patients at the time of conversion was 63 (range 27-91) years. Two hundred fifty were women and 54 were deceased. The median time until a patient started insulin therapy after failure of other treatments was 73 (12-360) months after diabetes diagnosis and 65 (4-360) months from their first visit at GP or DT. HbA1c

at time of conversion was 10% (7.2-17.9) and they spent 49 (0-325) months with HbA1c >7%, 25 (0-163) months with HbA1c >8% and 10 (0-135) months with HbA1c >9% which were 90%, 45% and 17% of their time under consultation respectively. HbA1c was 8.3% (5.2-15) at 12 months before conversion and decreased to 8.2% (5-14.7) at 12 months after conversion. There was a 2.9 kg [(-18.4)-(+11.7), p<0.05] increase in BW at 12 months after the initiation of insulin.

There was no difference in HbA1c level at the time of initiation of insulin between older and younger patients, but patients younger than 55 years were more overweight, 93.9 kg (43-166.6), were converted to insulin earlier (47 vs. 65 months) from their first consultation, and spent more time with uncontrolled diabetes (HbA1c >9%: 25.6 % of time vs. 11.9 % in patients older than 65 years) (Table 1).

The majority of patients (89.9%) started therapy with insulin analogues and continued with that. More than half were commenced an analogue mixture and the rest were treated with combination therapy (OAD + basal insulin) or with multiple day insulin therapy. There was a significant reduction in HbA1c (p<0.05) after the initiation of insulin at all age groups with all insulin regimen at 12 months but there was also a significant increase in BW(p<0.05).

Discussion

The UK National Institute for Clinical Excellence (NICE) guideline for T2DM in 2002 recommended an HbA1c target between 6.5% and 7.5%. The American Diabetes Association (ADA) followed in 2002 and 2004 suggesting HbA1c target below 8% and 7% respectively^{8,9}. However, despite the International Guidelines many patients with diabetes still have suboptimal control¹⁰. During the period 1997-2007 there was a very little improvement in UK national statistics for HbA1c which changed by only 0.1% from a mean HbA1c of 8.5% in 2001 to 8.4% in 2007¹¹. Our results are in agreement with previous studies showing that patients with T2DM are exposed to a significant glycemic burden before starting insulin therapy^{12,13}. Also, there was no difference in HbA1c level at the time of initiation of insulin between older and younger patients with diabetes. Patients younger than 55 years, although starting insulin earlier, spent more time with uncontrolled diabetes (25.6% of time with HbA1c >9% and 50 % with HbA1c >8%). This may reflect less motivation and greater reluctance to change therapy.

The majority of patients started with an insulin analogue, according to the protocols used at the time. After the initiation of insulin, there was a significant reduction in HbA1c at all age groups and with all insulin regimens at 12 months. In addition, more patients achieved a target of HbA1c below 7%, 8% or 9% at one year following the change in treatment compared to a year before the decision to start insulin (15.1% vs 8.8%, 46.1% vs. 34.2% and 7.4% vs. 6.6% respectively). Earlier intervention could be beneficial for these patients as it decreases the exposure to glycemic burden and this may have a positive

Table 1: Demographic and clinical data of the 509 patients from the Scottish Care Information-Diabetes Collaboration (SCI-DC) database, divided in three age groups (>65 years, ≤65 years, ≤55 years).

	Total patients	Group A >65 years	Group B ≤65 years	Group C ≤55 years
n	509	203	306	147
Male/female	263/246	93/110	271/135	73/74
Age (years)	63 (27-91)	73 (66-91)	56 (27-65)	49 (27-55)
HbA1c (%)				
-12 months	8.3 (5.2-15)	8.4 (5.4-14.7)	8.3 (5.8-15)	8.4 (6-15)
-6 months	8.8 (5.8-16.9)	8.6 (5.8-14) §	9 (6.6-16.9)	9.3 (6.6-16.9)
0 months	10 (7.2-17.9)	10 (7.7-17.9)	10 (7.2-16.6)	10.3 (7.4-16.6)
+6 months	8.4 (4.7-14.3)	8.3 (4.7-14.3)	8.4 (5.6-13.6)	8.6 (5.7-12.5)
+12 months	8.2 (5-14.7)	8 (5-13.1)	8.2 (5.5-14.7)	8.6 (6-14.7)
BW (kg)				
-12 months	89.4 (42.7-160)	80.8 (42.7-153.8) §	94 (44.1-160)	96.3 (44.1-154) *
-6 months	87.3 (39.2-168.9)	79.2 (39.2-154) §	93.2 (44.5-168.9)	95.1 (44.5-168.8) *
0 months	86.6 (39.6-179.8)	79.6 (39.2-153.8) §	91.4 (43-178.4)	93.9 (43-166.6) *
+6 months	88.6 (43.6-179.6)	81.5 (41.6-153.8) §	93.2 (43.9-179.6)	98.3 (43.9-160) *
+12 months	91 (42.7-196)	83.9 (46-146.6) §	94 (42.7-196)	97.3 (52.7-152) *
BMI (kg/m²)				
0 months	30.8 (15.8-58.1)	29.4 (18.2-54.3) §	32.3 (15.8-58.1)	33.3 (15.8-53.9) *
+12 months	32 (15.7-64.7)	30.3 (19.9-48.2) §	33.5 (15.7-64.7)	34.9 (15.7-52.4) *
Months to conversion from diagnosis	73 (12-360)	95(12-360) §	65 (12-248)	50 (12-153) *
Months to conversion from 1st visit	65 (4-360)	80 (5-360) §	55 (4-248)	47 (3-153) *
Months with HbA1c>7% % of time	49 (0-325) (90%)	55 (0-325) § (84.6%)	45 (1-221) & (92.8%)	33 (1-149) * (83.1%)
Months with HbA1c >8% % of time	25 (0-163) (45%)	26 (0-163) § (37%)	23 (0-154) (49.6%)	21 (0-135) * (50%)
Months with HbA1c> 9% % of time	10 (0-135) (17%)	9 (0-110) § (11.9%)	10 (0-135) (21,4%)	11 (0-135) * (25.6%)
Treatment				
Basal insulin n (%)	143 (28.1%)	73 (36.0%) §	70 (22.9%)	34 (23.1%) *
Mix insulin n (%)	323 (63.5%)	124 (61.1%)	199 (65.0%)	89 (60.5%)
Basal bolus n (%)	40 (7.9%)	4 (2.0%) §	36 (11.8%)	24 (16.3%) *
Analogous insulin n (%)	458 (89.9%)	175 (86.2%)	283 (92.5%)	138 (93.9%)
Metformin n (%)	344 (67.6%)	120 (59.1%) §	224 (73.2%)	122 (82.9%) *

Results are shown as median and range. Months before conversion to insulin are indicated as -6 months and -12 months. Months after conversion to insulin are indicated as +6 months and +12 months and the time of conversion is indicated as 0 months. n: number of patients, HbA1c: glycated hemoglobin, BW: body weight, BMI: body mass index, §: p<0.05 between groups A and B, *: p<0.05 between groups A and C, &: p<0.05 between groups B and C.

impact on microvascular complications.

An important barrier to achieve the glycemic targets is the delayed response of clinicians to antihyperglycemic treatment failure and the reluctance of patients to start insulin¹⁴⁻¹⁸. Clinicians typically begin to discuss, about insulin therapy, with their patients when HbA1c exceeds 9% but after that it takes almost a year for the commencement of therapy. In addition, clinicians focus only on the current HbA1c value and not on the duration of uncontrolled diabetes. Therapy should always be individualized and younger patients with short diabetes duration and no significant cardiovascular disease should have more stringent glycemic control¹⁴.

Limitations

The main limitation of the current study is its retrospective design, as there is no available data regarding complications, co-morbidities or symptoms that perhaps could affect clinicians' decisions to initiate insulin therapy. Moreover, there is no information regarding the factors that influenced both physicians and patients in delaying the change in therapy.

Conclusions

The current study shows that there is a gap between national and International Guidelines Recommendations and real-life clinical practice. There is a delay in the initiation of insulin therapy after other treatment failure re-

sulting in patients been exposed to prolonged period of hyperglycemia. After the initiation of insulin, there is a significant improvement in glycemic control but also an increase in BW. It is important to investigate the factors that act as barriers for insulin therapy initiation and perhaps a change in practical clinical guidelines is needed, in order to shorten the time period from patient's treatment failure to insulin therapy initiation.

Conflict of interest

Authors report no conflict of interest.

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