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Insulin initiation in primary care for patients with type 2 diabetes: 3-Year follow-up study

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ABSTRACT

Purpose of study: To evaluate the 3-year impact of initiating basal insulin on glycaemic control (HbA1c) and weight gain in patients with poorly controlled type 2 diabetes registered with UK general practices that volunteered to participate in an insulin initiation training programme.
Methods: Audit utilising data collected from practice record systems, which included data at baseline, 3, 6 months and subsequent six-monthly intervals post-insulin initiation for up to 10 patients per participating practice.
Results: Of 115 eligible practices, 55 (47.8%) contributed data on a total of 516 patients. The mean improvement in HbA1c levels in the first 6 months was 1.4% (range −3.8% to 8.2%, median = 1.40%). Thereafter, there was no overall change in HbA1c levels, although the change for individual patients ranged from −4.90% to +7.50%. At 36 months, 141 (41%) patients for whom data were provided had achieved the pre-2006/2007 UK Quality and Outcomes Framework (QOF) target of 7.4% or less, including 98 (29%) who had achieved an HbA1c of 7% or less. Patients who achieved target had a lower HbA1c at baseline (mean 9.1% compared to 9.7%; $p < 0.001$); had a lower weight at 36 months (mean 88.0 kg compared to 93.5 kg; $p = 0.05$); were more likely to be on basal insulin alone (88, 47.1% compared to 46, 34.6%; $p < 0.05$); and were slightly older (mean 64.5 years compared to 61.7 years; $p < 0.05$).
Conclusion: Attending an insulin initiation training programme may successfully prepare primary healthcare professionals to initiate insulin therapy as part of everyday practice for patients with poorly controlled type 2 diabetes. The impact on glycaemic control is maintained over a 3-year period. Although intensification of treatment occurred during this period, the findings suggest scope for further intensification of insulin therapy in order to improve on the glycaemic control achieved during the first 6 months post-insulin initiation.

1. Introduction

Tight glycaemic control is central to reducing the risk of long-term macrovascular and microvascular complications of type 2 diabetes and the associated morbidity and mortality [1]. The American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) [2], as well as the recent British National Institute of Clinical Excellence (NICE) guidelines on type 2 diabetes [3] recommend the addition of

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insulin for people with poorly controlled type 2 diabetes who are already on maximum tolerated doses of metformin and sulphonylurea. NICE recommends that this is the preferred management plan in those that are markedly hyperglycaemic.

Despite increasing recognition of the importance of insulin therapy, add-on or intensification of therapy often does not occur [4]. The failure of health care providers to intensify therapy has been partly attributed to clinical inertia [5], and there is evidence that this may be a particularly significant barrier to effective glycaemic control in primary care where clinicians may be less familiar with the need for, or process of, treatment intensification [6].

Until recently, in the UK people with type 2 diabetes requiring insulin were usually referred to secondary care for insulin initiation [7], but in recent years with the advent of training programmes for healthcare professionals working in the community insulin initiation in primary care has become more commonplace [4]. However, while there is much evidence of the improved glycaemic control and low risk of hypoglycaemia resulting from basal insulin therapy initiated in secondary care [8], the evidence is more limited about the broader applicability of this approach to patients in primary care. Specifically, there is little evidence on how long-term glycaemic control is maintained following the initiation of once daily basal insulin in primary care and the extent to which patients maintain target HbA1c levels over time.

Schreiber et al. [9] recently described a 9-month observational study, with an optional 20-month extension phase, that involved patients with inadequately controlled type 2 diabetes on oral therapy who were initiated on insulin glargine in everyday practice in Germany. Substantial improvement in glycaemic control was demonstrated without weight gain, and there were very few significant adverse events.

We recently reported findings from a 6-month audit of 115 UK general practices that had participated in an insulin initiation training programme [10]. Following training, participating general practitioners and practice nurses initiated basal insulin therapy for patients with poorly controlled type 2 diabetes. The audit demonstrated achievement of a mean reduction in HbA1c from 9.6% at baseline to 7.9% at 6-month follow-up with very few adverse events reported.

The aim of the current study was to describe the longer term impact on glycaemic control of insulin initiation in UK general practice by undertaking a follow-up audit with the same practices and patients recruited to our initial study. Here we describe how glycaemic control, weight gain, insulin dosage and oral therapy changed over the 3-year period following basal insulin initiation.

2. Methods

2.1. Setting

General practices throughout the UK.

2.2. Intervention

The Warwick Diabetes Care Intensive Management of type 2 diabetes programme is based on a 'training the trainer' type method in which two lead diabetes healthcare professionals from a locality are trained to facilitate a training approach to general practitioners and practice nurses in their area. The course involves learning through presentations, small group work, case studies and practical demonstrations to provide the knowledge and skills to facilitate intensified treatment of type 2 diabetes in general practice and insulin initiation (see Box1). It has been fully described elsewhere [10]. Between 2004 and 2006, a total of 607 practices participated from across the UK.

Box 1
The insulin initiation training approach
One day (or 2 half days) knowledge update on insulin initiation
Topics covered: insulins, delivery devices, insulin regimes and injection techniques Course participants, usually 10–14 individuals, including one GP and one practice nurse from each of a number of local practices.
Practical support offered in the practice
An experienced diabetes specialist nurse (DSN) supported practice nurses undertake their first insulin initiations. The first insulin initiation was undertaken by the DSN with practice nurse watching. The second and third were undertaken by the practice nurse with the DSN watching. If the practice nurse then felt confident, the DSN provided telephone contact and support for the following initiations.
Insulin titration algorithm
Initial dose = 10 units
In consultation with the practice nurse, the insulin dose was titrated by the patient on a weekly basis according to the mean of the last two fasting blood glucose measurements as follows:

Fasting blood glucose	Basal insulin dose increase
4.9–5.9 mmol	2 units
6.0–6.9 mmol	4 units
7.0–8.9 mmol	6 units
More than 8.9 mmol	8 units

The course taught that if once daily basal insulin alone was insufficient to get HbA1c to the target agreed with the patient a small dose of short acting insulin should be given with the main meal of the day. This could then be up-titrated according to blood glucose levels after the main meal. If one injection of short acting insulin in addition to basal insulin was insufficient a second injection of short acting insulin should then be given with the second largest meal of the day and up-titrated. If two injections of short acting insulin plus basal were insufficient a third dose of short acting insulin could be given, so getting to a full basal bolus regime.

2.3. Participants and data collection

All 115 practices that participated in the previous audit [10] were sent an invitation to provide data for the current study. Anonymised patient identifiers were sent to practices to enable them to report data on the same patients as were included in the previous audit. They were asked to provide data on HbA1c, weight, insulin regime and oral hypoglycaemic

therapy for each patient at up to eight points in time related to when insulin initiation occurred: baseline, 3, 6, 12, 18, 24, 30 and 36 months post-insulin initiation. In addition, they were asked to give details on any adverse events, such as a serious hypoglycaemic episode, that were recorded in patients' records. All data were returned to the study team in a fully anonymised format. No financial payments were made to practices.

2.4. *Data analysis*

The data were inputted into SPSS and analysed using descriptive statistics, analysis of variance (ANOVA), multiple regression and general linear modelling (GLM) [11]. GLM modelling was used to identify group and time interactions between insulin regimes. An audit report summarising the analysis of each practice's data was provided to the practice, together with comparisons about how the practice data compared to the wider study sample.

3. Results

Of the 115 eligible practices that participated in the first audit, 55 (47.8%) returned data. Nineteen (16.5%) failed to respond to the invitation to participate, 10 (8.8%) refused, and 31 (26.9%) initially agreed to participate but failed to return data within the timescale allowed despite at least two reminders; this appeared to be due to lack of time and/or financial reward.

As a result, data were returned on 516 patients. This included complete data (i.e. from all eight data collection points) on 338 (65.5%) patients, data from six or seven points on 42 (8.1%), data from four or five points on 27 (5.2%), and data from three of fewer points on 109 (21.1%) patients. Reasons for incomplete data included 44 (8.5%) patients who had died, 32 (6.2%) who moved practice, and 34 (6.8%) who could not be identified by the practice; no reasons were given for the remaining 68 (13.2%).

The age of patients in the current audit was similar to those in the previous audit: mean age 64.2 years (95% CI 61.8, 66.6) and 65.3 years (95% CI 64.5, 66.1) ($p = 0.089$).

3.1. *Insulin regime*

For patients about whom insulin dose was given ($n = 364$), the mean daily dose at 36 months was 58.5 IU/day (95% CI 54.8, 62.1; range 10–210). For 318 of these patients, information was provided on the type of insulin(s) being used: 184 (57.5%) patients were still on basal insulin alone, and 134 (42.5%) had additional shorter acting insulins incorporated.

3.2. *Oral glycaemic lowering agents*

Details of oral glycaemic lowering agents at 36 months were provided for 431 (83.5%) patients. Metformin was the most widely used agent (284; 66%), followed by sulphenylureas (87; 16.9%) and glitazones (13; 2.5%); 47 (11%) were reported as using other agents. Of these patients, 66 (15.3%) were reported as being on two oral agents, and one (0.2%) on all three.

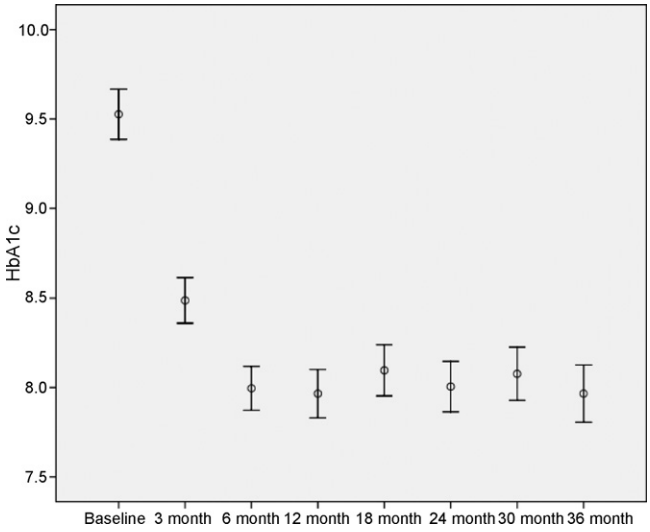

Fig. 1 – Mean with 95% confidence intervals for HbA1c levels over the 36-month period post-insulin initiation.

3.3. *Improvement in glycaemic control*

Fig. 1 shows how HbA1c levels changed over the 36-month period post-insulin initiation. The mean improvement in the first 6 months was 1.4% (range −3.8% to 8.2%, median = 1.4%), with HbA1c levels falling from a mean of 9.3% (95% CI 9.17, 9.43) at baseline to a mean of 7.9% (95% CI 7.78, 8.02) at 6 months. Thereafter, between months 6 and 36 there was no significant change overall, although for individual patients the change in HbA1c ranged from −4.90% to +7.50%. Multiple regression analysis including age, initial weight, type of insulin regimen and HbA1c levels at the various points in time as independent variables showed that the variables most strongly associated with the HbA1c level at 36 months were the HbA1c at 30 months (beta = 0.625) ($p = 0.000$) and HbA1c at 6 months (beta = 0.169) ($p = 0.003$).

As shown in Fig. 2, there was a persistent difference between the mean HbA1c levels for those patients who were still on basal insulin alone compared to those who by the final data collection point had been commenced on mixed insulins.

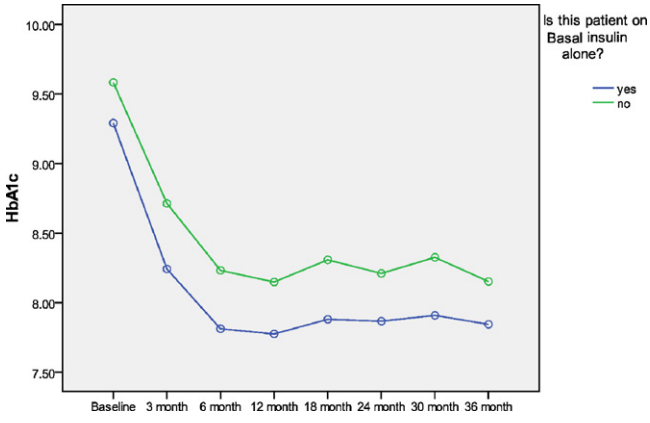

Fig. 2 – Mean HbA1c for patients on basal insulin alone compared to patients on mixed insulins.

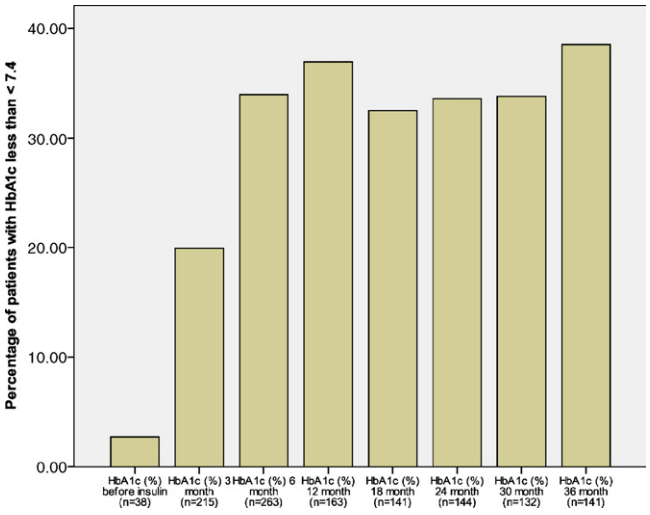

Fig. 3 – Proportion of patients with an HbA1c of 7.4% or less.

From the General Linear Model, this difference was significant ($p = 0.002$), as was the change in HbA1C over time ($p < 0.001$), but there was no interaction between them ($p = 0.944$) indicating that the change over time had the same pattern in both of the regimes.

The median HbA1c at 36 months for patients in the audit was equal to or less than 7.0% for 7 (12.7%) practices, between 7.1% and 7.5% for 14 (25.5%) practices, between 7.6% and 8.0% for 20 (36.3%) practices, and greater than 8.1% for 14 (25.5%) practices. The median HbA1c levels in the latter group of practices ranged from 8.1% to 10.7%. We tested for clustering using an ANOVA within- and between-practice test, including a random practice term, and found no significant effect for HbA1c at 36 months ($p = 0.117$).

3.4. *Achievement of target HbA1c*

Fig. 3 shows that the proportion of patients achieving the pre-2006/2007 Quality and Outcomes Framework (QOF) target HbA1C of 7.4% or less [12] showed little improvement from 6 months post-insulin initiation. At 36 months, 141 (41%) of the patients for whom data were provided had achieved this target, with 98 (29%) achieving an HbA1c of 7% or less. Analysis of variance revealed that the variables most strongly associated with achieving the target were HbA1c at baseline, weight at 36 months, insulin regime, and age. Patients who achieved target had a lower HbA1c at baseline (mean 9.1% compared to 9.7%; $p < 0.001$); had a lower weight at 36 months (mean 88.0 kg compared to 93.5 kg; $p = 0.05$); were more likely to be on basal insulin alone (88, 47.1% compared to 46, 34.6%; $p < 0.05$); and were slightly older (mean 64.5 years compared to 61.7 years; $p < 0.05$).

3.5. *Weight*

Patients' weight increased progressively from a mean of 88.0 kg (range 42.5–182.0, median 86.4) at baseline to a mean of 91.6 kg (range of 45.5–160.0, median 91.0) at 36 months. Comparing the first and last weight measurement for each patient, 289 (56%) patients gained weight (mean 6.45 kg), 145 (28%) lost weight (mean 4.29 kg), while 82 (16%) had no change.

3.6. *Adverse events*

Practices returned additional comments on 333 (64.5%) patients. In the main, these described changes in patients' clinical condition that occurred over the period (many related to cardio-vascular disease). Only two comments specifically related to hypoglycaemic attacks, of which one was reported as having led to hospital admission. Although a significant proportion of patients in the sample had died, none of these deaths were reported as having being related to insulin therapy.

4. Discussion

This study demonstrates maintenance over a 3-year period of the improvement in glycaemic control that occurs during the first 6 months following insulin initiation for poorly controlled type 2 diabetes. Comparing the findings from this audit with those from the previous audit, whereas at 6 months post-insulin initiation 95.3% of patients were being maintained on once daily insulin [10], by 36 months 42.5% now were using a combination of short and long acting insulins. The mean daily dose of insulin increased from 38.2 units at 6 months to 58.5 units at 36 months. Very few adverse events were reported. There was a slight increase in weight from a mean gain of 1.5 kg reported in the original audit to 3.6 kg after 36 months.

Together, these findings support the concept that healthcare professionals in UK general practice who have participated in a brief training course are able to initiate basal insulin therapy and intensify insulin therapy through the titration of dosages and the introduction of shorter acting insulins.

Although there was evidence that intensification of insulin therapy occurred over the 36-month period, in this cohort of patients the overall impact of such intensification was limited to maintaining the gains achieved in glycaemic control during the first 6 months. The proportion of patients achieving the target for glycaemic control showed little improvement between 6 months and 36 months. There was evidence that some practices achieved much greater improvement in their patients than did others. While 38.2% ($n = 21$) of practices reduced the median HbA1c of their audited patients to less than 7.5%, for 32.7% ($n = 18$) it remained at over 8.0%. Although there was no statistical evidence of clustering, it seems likely that practice-related attributes influenced the extent to which insulin intensification and improvement in glycaemic control occurred.

These finds are in line with those reported by Schreiber et al. [9] of insulin initiation in German everyday practice where glycaemic control was maintained to 21 months. However, in that study, the improvement in HbA1c was greater than observed here, in that by 6 months post-insulin initiation the HbA1c had dropped to a mean of 7.2%, a level of improvement that was maintained over the subsequent 21 months.

Very few critical incidents, such as serious hypoglycaemic episodes, were reported, but it is possible that some may have been overlooked. Likewise, very few patients in Schreiber et

al.'s study [9] experienced significant adverse events. Taken together, this provides encouraging support for the safety of insulin initiation in general practice by practitioners who have undergone training.

4.1. *Methodological limitations*

Methodological limitations associated with this audit study have been discussed previously [10]. Firstly, it was beyond the scope of this study to attempt validation of the patient data provided by individual practices. Secondly, the practices participating in the training were self-selected and the extent to which they were typical of other practices is unknown. As 'first wave' practices they may have had a greater level of knowledge and interest in diabetes than is typical of UK general practice. Thirdly, the findings are limited to practices that participated in one specific training programme, and so might not be applicable to other insulin initiation courses for primary care professionals. Finally, not all eligible practices reported data and this may limit the generalisability of the findings. However, the patients of the practices that did participate appeared to be representative of the cohort that participated in the original audit in terms of age and HbA1c levels at baseline and at 6 months. The absence of financial payments to cover the costs involved in reporting data for the audit appeared to have discouraged some practices' participation.

5. Conclusion

The findings from this audit indicate that the improvements in glycaemic control associated with commencing insulin treatment in general practice for patients with poorly controlled type 2 diabetes are maintained over the first 36 months. Although the study revealed evidence of ongoing insulin intensification, the proportion of patients that achieved target showed little improvement between 6 months and 36 months. It is possible that the first 6 months or so of insulin treatment may be the period when the motivation of both the patient and clinician are at their greatest to achieve glycaemic control within target. After this, further intensification appears to maintain the glycaemic control that have been achieved rather than improve upon it. There is a need for further research to understand the factors that influence the extent to which patients and general practice teams intensify insulin treatment, and further training and support may be needed to encourage additional improvements in glycaemic control.

The results of this study are relevant to general practice and will assist clinicians and policy makers develop improved services for people with type 2 diabetes. Changes in the QOF clinical indicators for glycaemic control in people with diabetes in the UK were introduced on 1 April 2009. To achieve maximum quality points, 50% of people in a practice registered as having diabetes now need an HbA1c of 7% or less, 70% need to have a HbA1c of 8% or less and 90% a HbA1c of 9% or less [13]. These tighter glycaemic control targets may well increase the need for practices to be trained in initiation of insulin and intensification of insulin therapy [14].

Conflict of interest

This research was supported by an unrestricted educational grant from Sanofi-Aventis. They also support the development and delivery of the "intensive management of type 2 diabetes programme".

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