

Chapter 4

Improving glycaemic control in patients with Type 2 diabetes mellitus without insulin therapy

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Abstract

Aims

In general practice at least 30% of those with Type 2 diabetes do not achieve good glycaemic control. We studied the effect of improving oral glucose-lowering medication in a primary care setting in patients treated with oral hypoglycaemic agents without satisfactory glycaemic control.

Methods

We provided flowcharts to general practitioners and outreach visits by trained facilitators, who checked adherence to the protocol. Fifty-two Dutch general practices with 2140 Type 2 diabetes mellitus (DM) patients recruited 288 patients \leq 75 years old inadequately controlled ($\text{HbA}_{1c} > 7\%$) by diet or oral medication. Outcome measures were decrease of HbA_{1c} , number of patients with $\text{HbA}_{1c} \leq 7\%$, and non-compliance rate.

Results

After a mean of 3.3 consultations over 14 weeks, 209 patients were following the protocol fully with a reduction in HbA_{1c} from 8.7% to 6.7% ($P < 0.001$). One hundred and fifty-eight patients (55%) achieved $\text{HbA}_{1c} \leq 7\%$, and 51 (18%) persisted with $\text{HbA}_{1c} > 7\%$ unless fasting blood glucose ≤ 7 mmol/l ($n = 18$) or a maximum of medication ($n = 33$). Seventy-nine patients (27%) did not adhere to the protocol, mostly due to loss of motivation and non-attendance.

Conclusions

A simple flowchart and relatively little support by trained facilitators results in improved glycaemic control.

Introduction

In patients with Type 2 diabetes even a small improvement in glycaemic control reduces the risk of diabetic complications.¹⁻³ In general practice, however, at least 30% of patients do not achieve the targets for good glycaemic control.⁴⁻⁸ Besides the unfavourable course of the disease,⁹ patient-related factors such as non-attendance¹⁰ and non-compliance with medication,¹¹ and on the part of general practitioners (GPs) inadequate management and treatment^{10,12,13} contribute to these outcomes. GPs often do not adjust treatments to achieve glycaemic targets, even with regular follow-up and review.¹⁴ For example, they may not prescribe adequate doses of oral hypoglycaemic agents. Insulin therapy is expensive and associated with lower health-related quality of life and treatment satisfaction,¹⁵ and it may be worthwhile maintaining normal glycaemia using oral agents. Guidelines

for diabetes treatment in primary care are available, but doctors often find them complex and feel they have insufficient staff to follow the recommendations.^{16,17}

We therefore investigated the effect on glycaemic control of encouraging GPs to adjust oral medication for Type 2 diabetes according to Dutch guidelines¹⁸ in patients with HbA_{1c} > 7%, by flowcharts and help from trained facilitators.

Patients and methods

The study was carried out in the Utrecht region between July 1999 and June 2000. Of 110 practices invited to take part, 52 (67 doctors) agreed to participate. Thirty-eight practices were single handed, of which 24 worked independently but sharing basic facilities in groups. Fourteen were practices run by either two or three doctors. The practices covered 131 000 people, including 2140 Type 2 diabetes patients (average per practice 41, crude prevalence 1.6%), and 1641 of these were treated in primary care. The medical ethical committee of the University Medical Centre of Utrecht approved the study.

Before the treatment protocol was introduced, the following data were collected from the medical records: medical history, glycaemic control (HbA_{1c} and fasting blood glucose), cardiovascular risk factors, treated in primary or secondary care, and presence of complications. Any data missing or outdated for the patients being treated in primary care were reported to the practices concerned, and their doctors were asked to complete the data sets by questioning and examining the patients.¹⁹

Patient selection and characteristics

The inclusion criteria were: treatment in primary care only; under age 76 years; treated with diet or hypoglycaemic agents or both; HbA_{1c} > 7.0% (measured by turbidimetric inhibition immunoassay Hitachi 917 (Roche Diagnostics, Basel, Switzerland); normal range 4–6%). Patients were excluded if they were already on maximal oral medication, required insulin therapy in the short term, or had severe co-morbidity. Patient selection is shown in Fig. 1.

Of 350 patients with HbA_{1c} > 7.0%, 62 were excluded because they were already on maximal oral medication (n = 27), insulin therapy was required (n = 12), serious co-morbidity in the opinion of the GP was present (n = 13), or for other reasons (moved, deceased, abroad, change of GP; n = 10). Examples of co-morbidity were: lung cancer, leukaemia, mental disorders, dementia, recent cerebral infarction, and pregnancy. The characteristics of the 288 patients eligible for the study are shown in Table 1. When compared with the

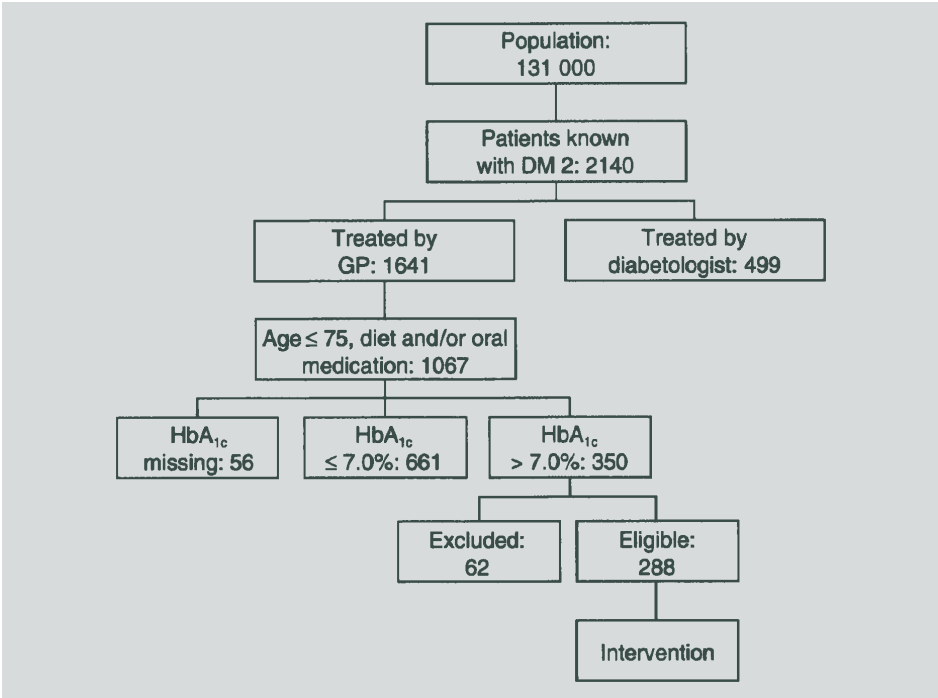


Figure 1 Patient selection. Absolute numbers.

Table 1 Characteristics of patients at baseline (n = 288)

Age (years)	59.9 (10.6)
Sex (male %)	45
Mean duration of diabetes (years)	4.6 (4.3)
Body mass index (kg/m ²)	29.2 (5.3)
HbA _{1c} (%)	8.8 (1.7)
Mode of treatment (%)	
Diet only	11
Sulfonylurea	40
Metformin	8
Sulfonylurea and metformin	39
Other	2

Results as means (SD) or percentages.

661 patients with good glycaemic control (HbA_{1c} ≤ 7.0%) (Fig. 1), the study group patients were of similar age and body mass index, had a longer duration of diabetes (4.6 vs. 3.1 years, P < 0.001), were less often on diet alone (11% vs. 34%, P < 0.001), and were more often treated with a combination of a sulphonylurea and metformin (39% vs. 18%, P < 0.001).

adjust oral medication according to the algorithm until either a fasting blood glucose concentration of ≤ 7.0 mmol/l was achieved or the maximum feasible dosages of the hypoglycaemic preparations in use were reached (depending on side-effects or contraindications). HbA_{1c} was measured 6 weeks after either of these targets had been reached, and oral medication had not been further adjusted. Two trained facilitators visited the practices every 3 weeks to check both patient and doctor compliance. Based on the previous audit by research assistants, the facilitators were informed about the eligible patients in every practice. During their visit they checked the progress of the consultations, and discussed the adherence to the flowchart's treatment and control schemes, as well as the correct adoption of the (maximum) daily dosages of oral hypoglycaemic agents (Fig. 2). They also supervised conscientious completion of the forms. Finally, in case patients did not show up, or exceeded the control interval of 2 weeks, practice assistants were asked to try to get defaulting patients to report in. When a patient did not adhere to the protocol treatment, doctors were asked to note the reasons on the form.

Statistical analysis

Data analyses were performed with SPSS release 10.0 (SPSS Inc., Chicago, IL, USA). Baseline and follow-up results were compared by paired *t*-tests. Patient related outcomes (HbA_{1c}) were calculated both in a per-protocol as well in an 'intent-to-treat' manner, assuming that patients lost to follow-up had no change in HbA_{1c} percentage. $P < 0.05$ was considered statistically significant.

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Results

The protocol was followed fully and HbA_{1c} measured in 209 patients, of whom 158 (55%) achieved good glycaemic control (HbA_{1c} $\leq 7.0\%$). Overall, mean HbA_{1c} decreased from 8.7% to 6.7% ($P < 0.001$). Including all eligible 288 patients, assuming that the 79 non-compliant patients had no change in HbA_{1c}, a 17% reduction in HbA_{1c} (8.8 to 7.3%; $P < 0.001$) was still achieved, while the number of patients with poor control (HbA_{1c} $> 8.5\%$) decreased from 126 to 51. The average number of consultations was 3.3 (range 1-10), while the average intervention period was 14.3 weeks per patient (1-49). Fewer patients at the end of the study than at baseline were being treated by diet alone (6%) or a single hypoglycaemic agent (36%), and more patients were being treated with two (56%) or three (2%) agents.

Of 51 patients (18%) with HbA_{1c} persistently over 7.0%, drug dosages had not been further adjusted in 18 because their fasting blood glucose concentrations were ≤ 7.0 mmol/l. In the remaining 33 patients the HbA_{1c} concentration was still $> 7.0\%$ in spite of a maximum dosage of oral hypoglycaemic treatment.

A total of 79 patients (27%) did not adhere to the protocol for the following reasons: loss of motivation or non-attendance ($n = 50$), referral to secondary care ($n = 4$), insulin therapy required ($n = 8$), language barrier ($n = 6$), or other reasons (moved, abroad, mental disorders, deceased, unknown; $n=11$). Compared with the 209 patients who completed the intervention, the 79 non-compliant patients were younger (56.5 vs. 60.4 years, $P < 0.01$), but other characteristics, such as HbA_{1c} at baseline, body mass index, duration of diabetes, and treatment, were similar (data not shown).

Discussion

The results of this study indicate that in general practice a simple flowchart supported by a limited number of outreach visits was successful in improving glycaemic control. The treatment and control schemes in this study were extracted from the Guideline on Type 2 diabetes from the Dutch College of General Practitioners,¹⁸ so they may be considered as 'recommended care'. In 209 patients in whom the intervention was fully applied we found a 23% reduction in mean HbA_{1c}. According to intention to treat, 55% of the patients reached good glycaemic control (HbA_{1c} $\leq 7.0\%$). As a result, in the initial population of 1067 patients under 76 years treated with diet and/or oral hypoglycaemic agents, the percentage with good glycaemic control increased from 62% to 77%. In 18 patients the HbA_{1c} remained above 7.0% in spite of fasting blood glucose ≤ 7.0 mmol/l. In clinical practice this is not uncommon in patients on diet or on oral hypoglycaemic drugs.²⁰ In such patients better control might have been achieved if the therapeutic algorithm had been based solely on regular HbA_{1c} measurements.

The mean number of consultations per patient was 3.3, during an average period of 14.3 weeks, so the instruction to measure glucose every 2 weeks in those with high values was not attained. A 2 weeks control scheme might be too tight, but compliance might improve in time as GPs and patients become more familiar with the approach.

Despite the combined efforts of facilitator, practice assistant and GP, the drop-out rate was quite high (27%, 79 patients), mostly due to lack of motivation of the patient. Patients who did not receive the maximum dose of oral agents (mostly metformin) because of side-effects were considered as having a maximum feasible dosage, and were not classified as dropouts. Our drop-out rates were comparable to other studies.¹⁰

It is probable that the outreach visits were important in improving glycaemic control. Based on the schedules from the facilitators, the 3-weekly visits took on average 1 h per practice, suggesting a rather modest time investment. It is noteworthy that an average general practice in the Netherlands (2500 patients)

is staffed by one GP and one practice assistant, which is probably insufficient to provide an adequate degree of diabetes care.²¹ In addition to following guidelines, additional support will be needed to improve diabetes care in general practice.

Important limitations need to be recognized when considering these data. With no control group, the net study effect might be influenced by other factors than just the intervention, such as 'regression to the mean' of HbA_{1c} values.²² Furthermore, the practices in this study were self-selected, reflecting a special interest in diabetes. Finally, the short duration of follow-up must be taken into account. In most patients, diabetes worsens over time,⁹ and most patients need multiple therapies to achieve good glycaemic control.²³ It is likely that the effect of our intervention will diminish. However, if both patients and practice staff can continue this approach, glycaemic control may be maintained.

The improvement in glycaemic control in our study is comparable to that found in several controlled studies aimed at improving glycaemic control with oral hypoglycaemic agents. DeFronzo and colleagues found in a randomized double-blind study that HbA_{1c} values improved an average of 1.5% after addition of metformin in patients whose diabetes was poorly controlled with diet or sulphonylurea therapy alone.²⁴ This was confirmed in the UKPDS, which studied the addition of metformin in suboptimally controlled overweight patients receiving maximum dosages of a sulphonylurea.²⁵ Gregorio and colleagues randomly assigned elderly Type 2 diabetes patients to a sulphonylurea up to maximum dosage or to addition of metformin, and found that HbA_{1c} declined 1.6% in both groups.²⁶ Notably, as in our study, this effect was achieved within 3 months, and was still present at 18 months. These studies as well as ours demonstrate that patients with poor control and inadequate therapy benefit from optimisation of oral medication irrespective of age, body mass index, or duration of diabetes. Both increasing the dosage in case of monotherapy and adding a second agent resulted in 1–2% lower HbA_{1c} concentrations, which should lead to fewer complications. In diabetic populations with worse control this approach might prove more successful. On the other hand, our results are in contrast to those of Frijling and colleagues,²⁷ in which a multifaceted and more elaborate intervention did not affect metabolic control. However, a systematic review of the effects of educational outreach visits showed positive results, especially on modifying prescribing.²⁸ Our experience may be useful in implementing current evidence-based treatment guidelines in daily practice and might be broadened towards the approach of other risk factors in patients with diabetes. This attitude can be promoted if support and interventions from health professionals such as facilitators or nurses are focused on both process and patient outcomes.²⁹

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