Control of Maturity-onset Diabetes by Monitoring Fasting Blood Glucose and Body Weight

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The feasibility of reducing the fasting blood glucose (FBG) level to <6 mmol/L has been studied in all 84 maturity-onset diabetic (MOD) patients in three general practices. Only 35 (48%) were initially "well controlled" by this criterion, although 72 (86%) had no postprandial glycosuria. Seventy-one patients were monitored for 6 mo. With additional oral hypoglycemic therapy where necessary, the number of "well controlled" increased from 29 (41%) to 54 (76%), associated with a significant decrease in the hemoglobin A_1. The patients were subsequently assessed at two 3-monthly intervals, and a fasting plasma glucose >4 and <6 mmol/L was usually maintained. All but two patients with a fasting glucose level <6 mmol/L had fasting triglyceride concentrations <2 mmol/L. The fasting blood glucose can be assayed in general practice with glucose-oxidase strips, and control by this means is simpler, cheaper, and more effective than regular urine glucose monitoring. DIABETES CARE 3: 607–610, SEPTEMBER–OCTOBER 1980.

The "control" of maturity-onset diabetes (MOD) is often assessed by urine glucose estimation or by random postprandial plasma glucose estimations. The height of the urine threshold, and the variability of postprandial hyperglycemia, makes it difficult to assess control accurately and to achieve normoglycemia by these means.

The raised postprandial glucose excursions of diabetes are superimposed on an increased basal plasma glucose concentration,[1–3] which is remarkably constant or "set" in each MOD individual in a given state of nutrition.[4] A logical aim of therapy is to reduce the basal hyperglycemia to normal, and this can often be achieved with ultralente insulin[3] or chlorpropamide.[5] The fasting plasma glucose concentration provides a simple and precise criterion of control in mild diabetes, although one has to take into account the slight increase of the plasma glucose concentration of fasting diabetic patients in response to exercise and stress (e.g., going to the hospital).[6] Fasting plasma glucose concentrations have been used as an index of diabetes,[7–9] but there is little information concerning the efficacy of control by monitoring primarily this abnormality, nor what is an appropriate level to aim for. The small day-to-day variation of fasting plasma glucose suggests that one could aim to lower the fasting plasma glucose concentration to <6 mmol/L.[10] This article reports experience with monitoring all MOD patients of three general practices by only the fasting blood glucose concentration and body weight.

PATIENTS AND METHODS

All 84 MOD patients in three general practices were studied. Their mean age was 65 yr (range 34–85 yr) and mean weight 24% over ideal weight (range −12 to 111) (Metropolitan Life Table). Thirty (36%) were on therapy with diet alone, 53 (63%) on therapy with sulfonylurea, and one on therapy with Ultratard M.C. insulin.[3]

Seventy patients were able to come fasting to a morning general practice clinic, whereas 14 were too infirm and needed a home visit. The fasting blood glucose was measured by Reflotest (Boehringer glucose-oxidase strips read on a Reflomat meter). Assay of duplicates showed a precision of ±0.25 mmol/L (±1 SD) and an accuracy compared with simultaneous plasma glucose assay by the Boehringer (GOD-perid) of ±0.47 mmol/L (±1 SD).[10] For home samples a nurse or doctor took the blood onto the strips, which were stored in a dessicant container before assay in the clinic.[10] All patients were asked to weigh themselves monthly, and to record the result on a "weight card."

If, in the absence of intercurrent illness, the initial fasting blood glucose was >6 mmol/L, therapy was increased to try to reduce the level to <6 mmol/L. Most patients were overweight and, in the first instance, further dietary advice was given, even to those who had previously failed to respond. Each was given a reasonable "target weight" to achieve or to maintain. Subsequently most patients required oral therapy and were started on chlorpropamide. The dose was increased

by up to a maximum of 500 mg or to 750 mg in patients weighing more than 75 kg. Patients who were on glibenclamide were given the drug twice daily, and the dose was increased up to a maximum of 10 mg b.d. If, with the maximal dose of either sulfonylurea, the blood glucose remained >6 mmol/L, Metformin up to 1000 mg/day was added. The patients were seen at 2-weekly intervals during the period of attempted control. Once the fasting blood glucose was measured at <6 mmol/L, or if fasting blood glucose remained >6 mmol/L on maximal therapy, the patients were seen at 3-monthly intervals. This study reports the subsequent progress up to 6 mo.

The hemoglobin A_1 (HbA_1) was assessed by column chromatography[11] at the initial assessment and 3 mo after "maximal" control had been achieved. Fasting plasma samples were assayed for triglyceride by the Boehringer kit at the same assessments. Statistics included paired and nonpaired Student's *t*-test.

RESULTS

At the initial assessment only 35 (48%) of patients had a fasting blood glucose of <6 mmol/L, even though 72 (86%) had previously had no postprandial glycosuria on routine testing either at previous clinic visits or at home. The mean fasting blood glucose was 8.2 mmol/L, with 14 patients having values >12 mmol/L. Of the 84 diabetic patients, it was only possible to study the response to more intensive monitoring and therapy in 71 patients, as 2 patients died from carcinomatosis, 3 had severe illnesses such that it was not reasonable to include them in the study, 2 had sufficiently severe diabetes that they were transferred to insulin with twice daily injections, 3 moved away from Oxford, and 3 patients refused to participate with fasting blood glucose monitoring. Twenty-nine (41%) of these 71 patients (11 on diet and 17 on oral hypoglycemic drugs and 1 on Ultratard insulin) initially had a fasting blood glucose <6 mmol/L.

In 54 (76%) patients a fasting blood glucose of <6 mmol/L was achieved, 13 patients with diet alone and 40 with additional therapies. Of the 25 patients who became "well controlled" (Figure 1), 10 were previously on sulfonylurea therapy, and their chlorpropamide dose was increased from a mean 150 to 300 mg/day. The 15 previously on diet achieved "control" on a mean dose of chlorpropamide of 200 mg/day. None of these 25 patients required additional Metformin. "Good control" was newly achieved after a mean of 2.9 visits (range 1–5).

Seventeen patients (24%) continued to have fasting blood

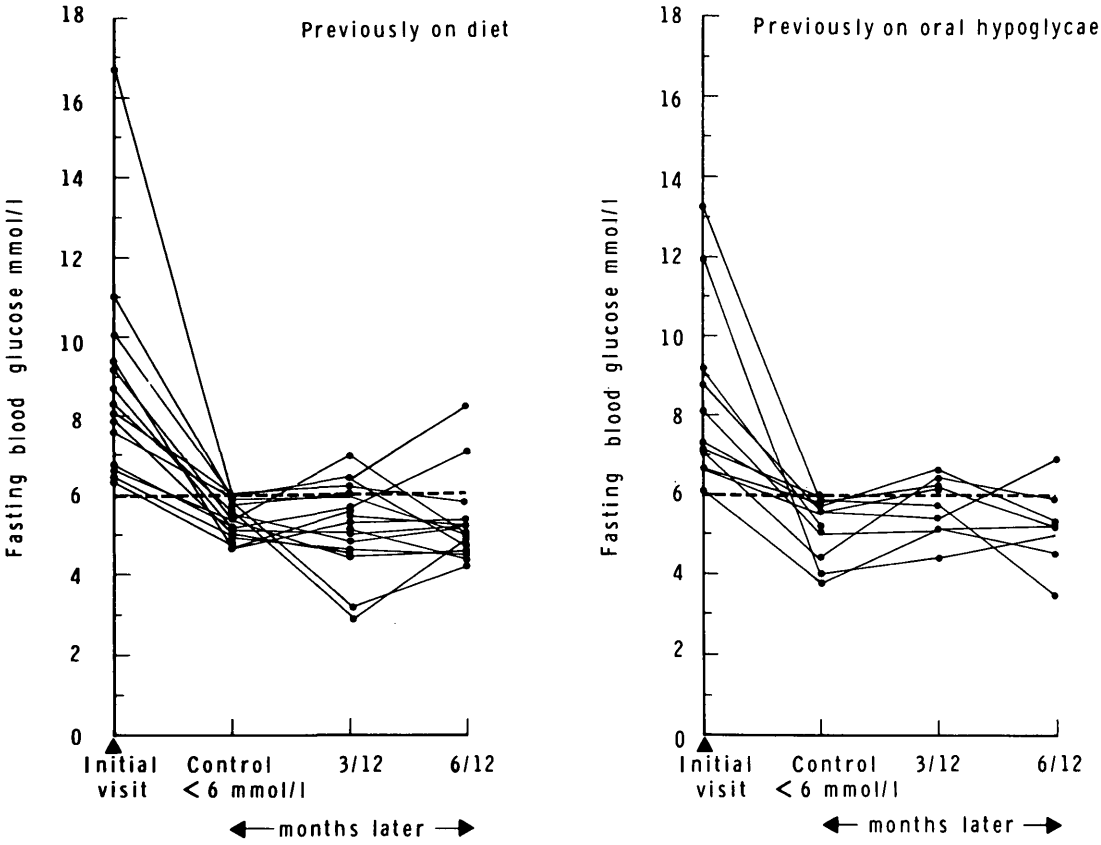

FIG. 1. The fasting blood glucose concentrations of 25 patients who initially had a value >6 mmol/L, and in whom <6 mmol/L was achieved, together with the subsequent values at 3-monthly intervals. The patients are subdivided into those who were initially on diet or had additional oral hypoglycemic therapy.

glucose >6 mmol/L on the maximal oral therapy and dietary advice, and these patients attended a mean of 4.2 visits (range 3–5) before "maximal" control was achieved. Nine patients were previously on chlorpropamide (mean dose 275 mg), 5 on glibenclamide (mean dose 15 mg/day), and 3 on diet. The addition of 1000 mg Metformin to maximal sulfonylurea therapy only decreased the fasting blood glucose by a mean of 1.1 mmol/L.

The majority of the patients, who either initially had a fasting blood glucose <6 mmol/L, or became <6 mmol/L, remained "well controlled," with the fasting blood glucose subsequently rising above 7 mmol/L in only 5 of 53 patients. On the other hand, all patients who initially failed to achieve "good control" continued to have raised fasting blood glucose concentrations. Figure 2 summarizes the change in blood glucose, HbA_1, and triglyceride in patients (1) who initially had a fasting blood glucose <6 mmol/L, (2) in whom this was newly achieved, and (3) in whom it was never achieved. The HbA_1 parallels the fasting blood glucose, and significantly improved in those patients in whom "good control" was newly achieved (mean ± 1 SD, 9.9 ± 1.7% to 8.7 ± 1.6%, $P < 0.02$) and in those in whom the fasting blood glucose remained >6 mmol/L ($P < 0.05$). The diabetic patients who were initially "well controlled" had a HbA_1 (8.4 ± 0.9%) significantly higher than in normal subjects (6.9 ± 1.2%, $P < 0.05$). Most patients with a fasting blood glucose <6 mmol/L also had normal fasting plasma triglyceride concentrations, only 2 out of 54 patients having a level >2 mmol/L.

A single blood glucose concentration >6 mmol/L, in the absence of an intercurrent illness, was used as a criterion for increasing oral therapy, and a fasting plasma glucose <4 mmol/L for reducing the dose. No patients had symptomatic hypoglycemia induced directly by increasing the dose. Only two patients had symptomatic hypoglycemia; both were obese and "well controlled" on chlorpropamide alone, but subsequently lost 8 and 12 kg weight, respectively, one because she later suddenly started a strict diet and one because of cancer. One patient had three hypoglycemic reactions during the day, but did not require hospital admission. The other had only vague symptoms of lethargy associated with a fasting blood glucose of 2.8 mmol/L. One Indian patient, who spoke and understood little English, had variable, high "fasting" blood glucose concentrations. It was not possible to determine if she fasted correctly before blood samples were taken. None of the patients with a fasting blood glucose <6 mmol/L had glycosuria at clinic visits.

The average weight of the patients decreased by 1 kg, there being no difference between the groups in whom "good control" was achieved or failed.

DISCUSSION

This study suggests that it is feasible to control MOD patients with only two criteria, the fasting blood glucose and the body weight. The decreased glycosylated hemoglobin provided an independent criterion that reduction of fasting blood glucose was associated with improved control. Patients who had a fasting blood glucose <6 mmol/L usually had normal triglyceride concentrations, and monitoring the fasting blood glucose appears to be an appropriate measure of overall diabetes control.

A control criterion of <6 mmol/L fasting blood glucose was set above the normal fasting blood glucose concentration, to allow for the day-to-day variation[10] and the increase in fasting blood glucose with the exercise of coming to the clinic.[6] As intermittent illness increases the fasting blood glucose concentration, the dose of a medication was only increased if the fasting plasma glucose was raised with the patient otherwise healthy. The aim of reducing the fasting blood glucose to between 4 and 6 mmol/L has been found to be clinically acceptable, with little risk of inducing clinical hypoglycemia. No episodes were induced by increased doses

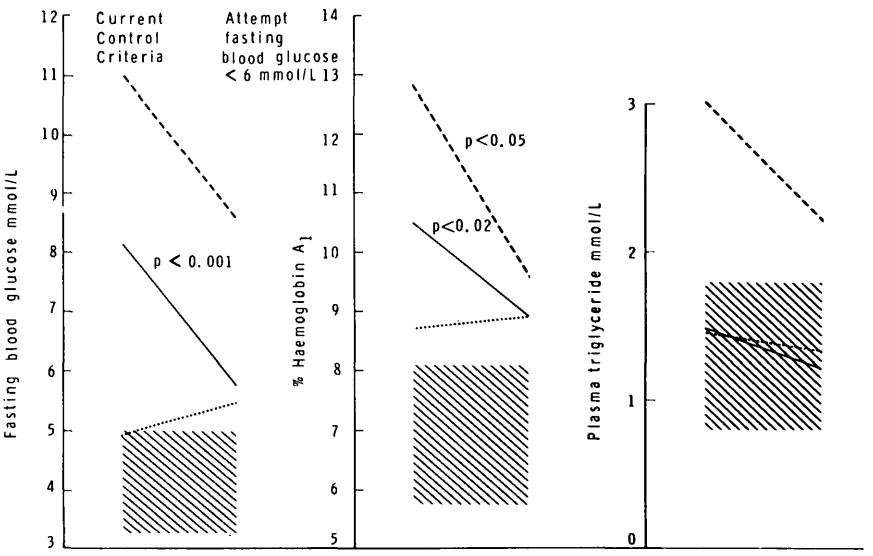

FIG. 2. The mean fasting blood glucose, HbA_1, and plasma triglyceride concentrations of three groups of patients: those in whom the blood glucose was initially <6 mmol/L (···), those in whom a blood glucose <6 mmol/L was newly achieved (——), and those in whom the blood glucose remained >6 mmol/L in spite of maximal oral hypoglycemic therapy (– – –). The shaded areas represent the normal range (±2 SD). At the 3-monthly follow-up the mean HbA_1 changed in parallel to the mean fasting blood glucose. The mean fasting plasma triglyceride remained raised in those patients in whom the fasting blood glucose remained raised.

of tablets, the only two episodes being in patients who had been "well controlled" but unexpectedly lost weight. Control by means of fasting blood glucose assay is not applicable in patients with an insufficient knowledge of English or comprehension because one cannot be certain that the patient has fasted before the blood sample was taken. The patients with a fasting blood glucose <6 mmol/L had a slightly raised HbA_1, which may be partly because their mean fasting blood glucose was still raised, and partly because on oral hypoglycemic therapy postprandial glucose concentrations are still raised, even if the basal plasma glucose concentration is normal.[5] About one in four MOD patients continued to have fasting blood glucose concentrations >6 mmol/L in spite of dietary advice and maximal oral hypoglycemic therapy.

In patients in whom the fasting blood glucose is maintained at <6 mmol/L, there is usually no glycosuria, and there is no need to test their urine for glucose routinely. This "unpleasant" procedure can be reserved for when the patient is ill or feeling unwell, as a "fail-safe" to detect loss of diabetes control. Patients were asked to weigh themselves at monthly intervals, and a "weight card" provided an additional reminder to the patients to keep to their diet and to try to obtain a target weight. We followed patients at 3-monthly intervals, and in general this interval appears to be appropriate. Patients with mild diabetes in whom a fasting blood glucose concentration of <6 mmol/L can be achieved by diet alone or with low doses of tablets could probably be seen at 6-monthly if not yearly intervals. On the other hand, patients with raised fasting blood glucose concentrations can be seen more frequently, and we saw patients at 2–4-weekly intervals when trying to improve control. Thus, as with hypertension, the frequency of monitoring control could depend upon the severity of the disease and the ease with which control can be maintained.

The use of the single, easy to understand, and precise index of the fasting blood glucose concentration simplifies the control of MOD. Patients treated with sufficient chlorpropamide to produce normal fasting plasma glucose concentrations still have high postprandial levels,[5] and clear-cut criteria for control based on such measurements are not available. Monitoring fasting blood glucose allows improved control in patients who have no glycosuria but continued basal hyperglycemia. The method is applicable to general practice, and most patients preferred the convenience of attending their local doctor rather than coming to a hospital. While a general practitioner could take a blood glucose for a laboratory estimation, the Reflotest/Reflomat glucose-oxidase system provided sufficiently precise results, with the immediate availability of the result assisting therapeutic decisions. This method of monitoring therapy is cheaper than patients testing their own urine or coming to a hospital clinic. Thus, four Reflotest strips per year cost the same as 40 urine tests. A visit to a general practitioner costs the Health Service one-fifth of a visit to a hospital doctor in an out-patient clinic, and a home visit by a district nurse to take a fasting blood glucose costs one-tenth of sending the patient by ambulance to a hospital clinic.[12]

The improved control may help to prevent episodes of overt diabetes precipitated by intercurrent infections, and theoretically might help to retard the progress of diabetic tissue damage.

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