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Impact of fasting and postprandial glycemia on overall glycemic control in type 2 diabetes Importance of postprandial glycemia to achieve target HbA1c levels

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Abstract

Objective: HbA1c values reflect overall glycemic exposure over the past 2–3 months and are determined by both fasting (FPG) and postprandial plasma glucose (PPG) levels. Cross-sectional studies suggest that attainment of HbA1c goals requires specific targeting of postprandial hyperglycemia.
Research design and methods: We undertook a prospective intervention trial to assess the relative contribution of controlling FPG and PPG for achieving recommended HbA1c goals. One hundred and sixty-four patients (90 male and 74 female) with unsatisfactory glycemic control (HbA1c $\geq$7.5%) were enrolled in an individualized forced titration intensified treatment program.
Results: After 3 months HbA1c levels decreased from 8.7 ± 0.1 to 6.5 ± 0.1% ($p < 0.001$); FPG decreased from 174 ± 4 to 117 ± 2 mg/dl ($p < 0.001$); PPG decreased from 224 ± 4 to 159 ± 3 mg/dl ($p < 0.001$) and daylong hyperglycemia (average of premeal, postprandial and bedtime plasma glucose excluding FPG) decreased from 199 ± 4 to 141 ± 2 mg/dl ($p < 0.0001$). Patients' weight remained unchanged (84.0 ± 1.4 kg versus 82.9 ± 1.5 kg, $p = 0.36$). No severe hypoglycemia occurred. Only 64% of patients achieving FPG targets of <100 mg/dl achieved an HbA1c target of <7% whereas 94% of patients achieving the postprandial target of <140 mg/dl did. Decreases in PPG accounted for nearly twice as much for the decreases in HbA1c as did decreases in FPG. PPG accounted ~80% of HbA1c when HbA1c was <6.2% and only about 40% when HbA1c was above 9.0%.
Conclusions: Control of fasting hyperglycemia is necessary but usually insufficient for achieving HbA1c goals <7%. Control of postprandial hyperglycemia is essential for achieving recommended HbA1c goals.
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1. Introduction

Controlled clinical trials have demonstrated that reducing HbA1c lessens the risk of micro- and macrovascular complications for patients with type 2

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diabetes [1–4]. The American Diabetes Association currently recommends HbA1c levels of ≤7.0% [5]. The International Diabetes Federation [6] and American Association of Clinical Endocrinologists [7] recommend a target of ≤6.5% based on evidence that more strict glycemic control might be necessary to prevent macrovascular complications [1,8,9].

HbA1c levels reflect overall glycemic exposure over the past 2–3 months and are determined by both fasting and postprandial plasma glucose (PPG) exposure. Cross-sectional studies suggest that attainment of recommended HbA1c goals of <7.0 or 6.5% may require specific targeting of postprandial hyperglycemia [10,11].

We therefore undertook a prospective study to assess the relative contribution of controlling fasting and postprandial hyperglycemia in achieving recommended HbA1c goals. One hundred and sixty-four patients with type 2 diabetes having HbA1c levels >7.5% were treated for 3 months with individualized forced titration regimens designed to reduce their FPG to ≤100 mg/dl and their 90 min postmeal plasma glucose to ≤140 mg/dl. Our results indicate that targeting postprandial hyperglycemia is essential to optimise glycemic control and that this can be achieved without either unacceptable weight gain or increased risk for severe hypoglycemia.

2. Methods

One hundred and sixty-four subjects (90 male and 74 female) with suboptimal glycemic control (HbA1c levels >7.5%) were enrolled in the study after giving informed consent. Demographic characteristics and treatment regimens before and after 3 months are given in Table 1.

At the first clinic visit venous blood samples were obtained for determination of HbA1c levels. Subjects were trained to use a self monitoring blood glucose device (Ascensia elite, Dex 2, Bayer, Accu-Chek Comfort, Free Style, Roche Diagnostics) and accuracy of measurements was ascertained once with a plasma glucose analyser of laboratory quality (Hemocue, AB, Aengelholm, Sweden, coefficient of variation 2.3%, range 30–400 mg/dl) [12]. Patients were advised not to eat more than three carbohydrate containing meals per day and to measure a seven-point diurnal blood glucose profile thereafter before any further treatment modifications. Three preprandial measurements at ∼7 a.m., 1 p.m. and 7 p.m. and three postprandial measurements 90 min after completion of each meal and a measurement at bedtime at ∼11 p.m. were obtained. Values 90 min after meal completion are henceforth referred to as postprandial and the average of all accept fasting values is referred to as daylong glycemia.

Subsequently each individual participated in a 1 week structured diabetes training program including seven 90 min sessions focused on life style intervention such as reduction in calorie intake, avoidance of rapidly absorbed carbohydrates as well as high fat and high protein consumption and the importance of physical activity. In additional sessions special attention was put on the individual therapy, i.e. optimal timing and technique of drug administration, effects of medications on plasma glucose regulation and the potential to cause hypoglycemia. During this week each individual obtained daily blood glucose profiles and was seen by a physician in order to select or adjust their treatment regimen. All major therapy modifications took place within the initial two weeks. Patients were initially seen at least three to four times a week until goals of therapy were achieved; thereafter they were seen at least once a month until the end of the study period.

Cut-offs for fasting and postprandial plasma glucose concentrations were based on IDF recommendations for self measured whole blood glucose concentrations of 100 and 140 mg/dl.

Table 1
Demographic characteristics and treatment regimens before and after 3 months

Age (years)	62.4 ± 0.9
Gender	90 men/74 women
BMI (kg/m^2)	28.8 ± 0.6
Diabetes duration (years)	8.4 ± 0.6

	Initial treatment (%)	Final treatment (%)
Diet alone	42 (26)	7 (4)
Metformin alone	17 (10)	17 (10)
Secretagogue alone	32 (20)	15 (9)
Metformin plus secretagogue	23 (14)	11 (7)
NPH-insulin alone	5 (3)	12 (7)
NPH plus metformin	6 (4)	14 (9)
NPH plus secretagogue	13 (8)	34 (21)
Twice insulin	1 (1)	1 (1)
NPH plus short acting insulin	19 (12)	34 (21)
NPH plus short acting insulin plus metformin	2 (1)	4 (2)
NPH plus secretagoge plus metformin	4 (2)	15 (9)

3. Overview of approach

The initial goal of therapy intensification was aimed at achieving an FPG of <100 mg/dl. If initial FPG was >100 but <140 mg/dl on diet alone, metformin was given. If on a sulfonylurea metformin was added. If FPG <100 mg/dl was not achieved on metformin with or without a sulfonylurea NPH insulin at bedtime was initiated and titrated based on FPG levels and the sulfonylurea was discontinued. NPH-insulin was injected in the thigh since this prolongs the duration of the insulin.

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