

Targeting postprandial blood glucose concentrations reduced haemoglobin A_{1c} concentrations in type 2 diabetes mellitus

Bastyr EJ 3d, Stuart CA, Brodows RG, et al, for the IOEZ Study Group. *Therapy focused on lowering postprandial glucose, not fasting glucose, may be superior for lowering HbA_{1c}*. *Diabetes Care* 2000 Sep;23:1236–41.

QUESTION: What is the comparative efficacy and safety of treatment strategies that target either fasting, premeal, or postprandial glucose concentrations in patients with type 2 diabetes mellitus that was not adequately controlled with sulfonylurea agents alone?

Design

Randomised [allocation concealed*]†, unblinded,* controlled trial with 3 months of follow up.

Setting

22 centres in the US.

Patients

135 patients (mean age 57 y, 60% men) with type 2 diabetes who had secondary sulfonylurea failure defined as initial stabilisation of glucose control for ≥6 months and a subsequent lack of glucose control using maximal sulfonylurea doses. 114 patients (84%) had complete follow up.

Intervention

Patients were allocated to 1 of 3 groups for 3 months: insulin lispro plus glyburide (L plus G group, n=41), which targeted postprandial blood glucose concentrations; metformin plus glyburide (M plus G group, n=40), which targeted premeal glucose concentrations; or NPH insulin plus glyburide (NPH plus G group, n=50), which targeted fasting glucose concentrations. For all 3 groups, glyburide was given as 10 mg by mouth twice daily. Insulin lispro was given subcutaneously in divided doses before meals starting at 0.25 U/kg per day. Metformin was given starting at 500 mg by mouth twice daily. NPH insulin was given subcutaneously at bedtime starting at 0.2 U/kg. Dose adjustments were made as necessary.

Main outcome measures

Blood glucose concentrations, haemoglobin (Hb) A_{1c} concentrations, rate of hypoglycaemic episodes, and patient satisfaction with treatment.

Main results

The mean HbA_{1c} concentration was lower for the L plus G group (7.7%) than for the NPH plus G group (8.5%, p=0.003) or the M plus G group (8.3%, p=0.025). The mean fasting blood glucose concentration was lower for the NPH plus G group (8.5 mmol/l) than for the L plus G group (10.6 mmol/l, p<0.001) or the M plus G group (9.7 mmol/l, p=0.03). The mean 2 hour postprandial glucose concentration after a test meal was lower for the L plus G group (10.9 mmol/l) than for the NPH plus G group (12.2 mmol/l, p=0.05) or the M plus G group (12.7 mmol/l, p=0.009). The groups did not differ for rates of hypoglycaemic episodes or patient satisfaction with treatment.

Conclusion

A combination regimen with insulin lispro plus glyburide that targeted postprandial blood glucose concentrations was well tolerated and lowered haemoglobin A_{1c} concentrations more than regimens that targeted fasting blood glucose concentrations in patients with type 2 diabetes that was not adequately controlled with sulfonylurea treatment alone.

*See glossary.

†Information provided by author.

COMMENTARY

Clinical trials consistently support tight glycaemic control to reduce or delay diabetes related microvascular complications. Strategies to achieve this control are limited by adherence to complex treatment regimens, adverse effects, and the burdens of living with chronic disease.

Clinical practice traditionally targets fasting glycaemic control. This practice has been motivated, in part, by glucose lowering medications with convenient dosing intervals that reduce fasting and premeal glucose concentrations, have acceptable side effects, and promote adherence. The results of the trial by Bastyr *et al* suggest that the focus should shift to postprandial hyperglycaemia.

This short term study supports the hypothesis that postprandial glycaemic control contributes to improvements in HbA_{1c} concentration and suggests that this contribution is larger than that of fasting glycaemic control. The study is limited by the lack of blinding and the number of patients who discontinued (17 of 135), although only 4 of 135 were excluded from the final analysis because of not meeting inclusion criteria. However, the results are concordant with other physiological, clinical, and epidemiological research.

Achieving fasting and postprandial glycaemic control may lower the risk for microvascular complications.¹ The contributions of postprandial glycaemic control in lowering this risk are unknown. Available regimens targeting postprandial glucose concentrations require patient effort, such as the use of multiple administrations of insulin or oral agents, which is difficult to sustain. High quality trials and simpler regimens may help to convince patients and clinicians that focusing on postprandial glycaemic control is worth the effort.

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1 Ohkubo Y, Kishikawa H, Araki E, *et al*. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. *Diabetes* 1995;28:103–17.

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