

# Targeting postprandial blood glucose levels reduced hemoglobin A<sub>1c</sub> levels 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<sub>1c</sub>. *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 levels in patients with type 2 diabetes mellitus that was not adequately controlled with sulfonylurea agents alone?

## DESIGN

Randomized {allocation concealed\*}†, unblinded,\* controlled trial with 3-month follow-up.

## SETTING

22 centers in the United States.

## PATIENTS

135 patients (mean age 57 y, 60% men) with type 2 diabetes who had secondary sulfonylurea failure defined as initial stabilization of glucose control for  $\geq 6$  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 levels; metformin plus glyburide (M plus G group,  $n = 40$ ), which targeted premeal glucose levels; or NPH insulin plus glyburide (NPH plus G group,  $n = 50$ ), which targeted fasting glucose levels. 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 levels, hemoglobin (Hb) A<sub>1c</sub> levels, rate of hypoglycemic episodes, and patient satisfaction with treatment.

## MAIN RESULTS

The mean HbA<sub>1c</sub> level 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 level 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 level 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 hypoglycemic episodes or patient satisfaction with treatment.

## CONCLUSION

A combination regimen with insulin lispro plus glyburide that targeted postprandial blood glucose levels was well tolerated and lowered hemoglobin A<sub>1c</sub> levels more than did regimens that targeted fasting blood glucose levels in patients with type 2 diabetes that was not adequately controlled with sulfonylurea treatment alone.

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\*See Glossary.

†Information provided by author.

## COMMENTARY

Clinical trials consistently support tight glycemic 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 glycemic control. This practice has been motivated, in part, by glucose-lowering medications with convenient dosing intervals that reduce fasting and premeal glucose levels, have acceptable side effects, and promote adherence. The results of the trial by Bastyr and colleagues suggest that the focus should shift to postprandial hyperglycemia.

This short-term study supports the hypothesis that postprandial glycemic control contributes to improvements in HbA<sub>1c</sub> level and suggests that this contribution is larger than that of fasting glycemic 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 of this trial are concordant with other physiologic, clinical, and epidemiologic research.

Achieving fasting and postprandial glycemic control may lower the risk for microvascular complications (1). The contributions of postprandial glycemic control in lowering this risk are unknown. Available regimens targeting postprandial glucose levels 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 glycemic control is worth the effort.

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## Reference

- 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.