A randomized double-blind trial of acarbose in type 2 diabetes shows improved glycemic control over 3 years (U.K. Prospective Diabetes Study 44)

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OBJECTIVE: To determine the degree to which alpha-glucosidase inhibitors, with their unique mode of action primarily reducing postprandial hyperglycemia, offer an additional therapeutic approach in the long-term treatment of type 2 diabetes. RESEARCH DESIGN AND METHODS: We studied 1,946 patients (63% men) who were previously enrolled in the U.K. Prospective Diabetes Study (UKPDS). The patients were randomized to acarbose (n = 973), titrating to a maximum dose of 100 mg three times per day, or to matching placebo (n = 973). Mean +/- SD age was 59 +/- 9 years, body weight 84 +/- 17 kg, diabetes duration 7.6 +/- 2.9 years, median (interquartile range) HbA1c 7.9% (6.7-9.5), and fasting plasma glucose (FPG) 8.7 mmol/l (6.8-11.1). Fourteen percent of patients were treated with diet alone, 52% with monotherapy, and 34% with combined therapy. Patients were monitored in UKPDS clinics every 4 months for 3 years. The main outcome measures were HbA1c, FPG, body weight, compliance with study medication, incidence of side effects, and frequency of major clinical events. RESULTS: At 3 years, a lower proportion of patients were taking acarbose compared with placebo (39 vs. 58%, $P < 0.0001$), the main reasons for noncompliance being flatulence (30 vs. 12%, $P < 0.0001$) and diarrhea (16 vs. 8%, $P < 0.05$). Analysis by intention to treat showed that patients allocated to acarbose, compared with placebo, had 0.2% significantly lower median HbA1c at 3 years ($P < 0.001$). In patients remaining on their allocated therapy, the HbA1c difference at 3 years (309 acarbose, 470 placebo) was 0.5% lower median HbA1c (8.1 vs. 8.6%, $P < 0.0001$). Acarbose appeared to be equally efficacious when given in addition to diet alone; in addition to monotherapy with a sulfonylurea, metformin, or insulin; or in combination with more complex treatment regimens. No significant differences were seen in FPG, body weight, incidence of hypoglycemia, or frequency of major clinical events. CONCLUSIONS: Acarbose significantly improved glycemic control over 3 years in patients with established type 2 diabetes, irrespective of concomitant therapy for diabetes. Careful titration of acarbose is

needed in view of the increased noncompliance rate seen secondary to the known side effects.