The Fasting Hyperglycaemia Study: III. Randomized controlled trial of sulfonylurea therapy in subjects with increased but not diabetic fasting plasma glucose.

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Self-referred subjects (N = 227) thought to be at increased risk of developing diabetes who had fasting plasma glucose (FPG) values in the range of 5.5 to 7.7 mmol.L-1 on two consecutive occasions 2 weeks apart were randomized to sulfonylurea therapy (gliclazide, < or = 160 mg.d-1) or to a control group allocated either to double-blind placebo or to no tablets. Subjects were randomly allocated also to reinforced or basic healthy-living advice in a factorial design. A total of 201 subjects have been evaluated for 1 year in three English and two French hospital outpatient centers. Those allocated to sulfonylurea had a significant (P < .001) reduction in median FPG compared with the control group (6.0 mmol.L-1 to 5.6 mmol.L-1, P < .001, v 6.0 mmol.L-1 to 6.0 mmol.L-1, NS). Median hemoglobin A1c (HbA1c) also improved (P < .0002; 5.8% to 5.6%, P < .001, v 5.7% to 5.6%, NS), as did mean beta-cell function (62% to 70%, P < .01, v 62% to 61%, NS). Mean body weight was unchanged in subjects allocated to sulfonylurea (81.7 kg to 82.4 kg, NS), but decreased in the control group (81.6 kg to 80.4 kg, P < .01). More subjects in the sulfonylurea group versus the control group reported one or more minor symptoms of hypoglycemia over 1 year (50% v 24%, P < .0001). Only two subjects reported major hypoglycemic episodes requiring assistance, both of whom were taking sulfonylurea. Insulin sensitivity did not change between groups. Sulfonylurea therapy with gliclazide improved glycemic control and beta-cell function significantly in subjects with increased but not diabetic FPG levels. The study is being extended to determine whether sulfonylurea therapy prevents progression to non-insulin-dependent diabetes mellitus (NIDDM).