Sulphonylurea therapy over six years does not delay progression to diabetes

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Background and Aims: Dysglycaemia is a risk factor for cardiovascular disease and type 2 diabetes. We aimed to determine whether sulphonylurea therapy could prevent or delay progression to diabetes in subjects thought to be at risk with two successive fasting plasma glucose (FPG) 5.5 to 7.7 mmol/L.
Materials and Methods: 188 subjects were randomised in a double blind, prospective study, 50% to gliclazide (maximum 320 mg daily) and 50% to control (placebo 25%, no tablets 25%). Simultaneously subjects were randomised in a factorial design, 50% to reinforced and 50% to basic healthy living advice. Mean (SD) age was 50 (9) years, weight 81.7 (14.5) kg, median (IQR) FPG 5.9 (5.6 to 6.3) mmol/L, two hour OGTT plasma glucose (2HPG) 9.0 (6.8 to 11.0) mmol/L. 7% had FPG $\geq$ 7.0 mmol/L and 45% were male.
Results: Tablet compliance did not differ between groups. Three subjects allocated to gliclazide reported severe hypoglycaemic episodes. Over six years fewer subjects in the gliclazide (3.2%) than the control group (10.8%) became overtly diabetic with two successive FPG values > 10 mmol/L ($p = 0.047$). There was no difference in the proportion with two successive values $\geq$ 7.8 mmol/L (17% *vs* 18%) or the proportion undergoing an OGTT at 6 years (n = 109) who were diabetic (54% *vs* 42%, WHO 1985 criteria). In the gliclazide, compared to the control group, there was a net reduction in fructosamine (7 µmol/L, $p = 0.033$), net increase in weight (4.1 kg, $p < 0.0001$) and 2HPG (1.8 mmol/L, $p = 0.0004$) but no significant differences in FPG, HbA_{1c}, lipid profiles, HOMA derived beta cell function or insulin sensitivity. Following a two month therapy washout there was a net increase in FPG (0.3 mmol/L, $p = 0.022$) and fructosamine (16 µmol/L, $p = 0.0003$) in the gliclazide group (n = 54) compared to the control group (n = 38) but no significant differences in weight, 2HPG, HbA_{1c}, or the proportion with diabetes.
Conclusion: Six years' gliclazide therapy did not delay progression to diabetes in these at risk subjects with median FPG 5.9 mmol/L.