UKPDS 26: Sulphonylurea failure in non-insulin-dependent diabetic patients over six years. UK Prospective Diabetes Study (UKPDS) Group.

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Patients with Type 2 (non-insulin-dependent) diabetes mellitus (DM) on sulphonylurea therapy convert to insulin progressively as the sulphonylureas 'fail'. The rate of failure and the features of those who fail have been poorly described. To assess secondary failure rates of sulphonylureas, we report on the responses in 1305 patients with newly diagnosed Type 2 DM randomly allocated to therapy with either chlorpropamide or glibenclamide in the UK Prospective Diabetes Study (UKPDS). These patients were initially treated by diet for 3 months and had a fasting plasma glucose > 6 mmol l(-1); mean age 53 (SD 9) years; BMI 26.8 (SD 5.0) kg m(-2); and median fasting plasma glucose 9.1 (7.6-12.5 quartiles) mmol l(-1). If their fasting plasma glucose subsequently rose above 15.0 mmol l(-1), or they developed hyperglycaemic symptoms, additional hypoglycaemic therapy was given: metformin, ultratard insulin, and soluble insulin as required. By 6 years, 44% had required additional therapy. Of those randomized to glibenclamide, 48% required additional therapy by 6 years, compared with 40% of those allocated to chlorpropamide ($p < 0.01$). Sixty-one per cent, 39%, and 23%, respectively, of patients with fasting plasma glucose > or = 10.0 mmol l(-1), > or = 7.8 mmol l(-1) to < 10.0 mmol l(-1) and < 7.8 mmol l(-1) at randomization required additional therapy ($p < 0.001$). In the initial 3 years, non-obese subjects (BMI < 30 kg m(-2)) were more likely to require additional therapy than obese patients (BMI > or = 30 kg m(-2)) (43% vs 53% at 6 years; $p < 0.001$). Modelled beta-cell function showed that those with lower function were more likely to fail ($p < 0.0001$). Thus sulphonylureas fail as a therapeutic agent at rates which are dependent both on the phenotype at presentation and perhaps on the agent used initially. Higher failure rates were found in those with higher glucose concentrations, those who were younger, those with lower beta-cell reserve and those randomized to glibenclamide compared with chlorpropamide.