Drugs 2002; 62 (9): 1365-1366
0012-6667/02/0009-1365/$30.00/0

Gliclazide Modified Release

A Viewpoint by Pierre-Jean Guillausseau

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Type 2 diabetes mellitus results from the association of insulin deficiency, mainly inherited, and decreased insulin sensitivity, mainly due to environmental factors. These metabolic alterations lead to the chronic hyperglycaemia responsible for micro- and macroangiopathy and neuropathy. Treatment of patients with type 2 diabetes mellitus aims to control both long-term blood glucose levels and cardiovascular risk factors (hypertension, high serum low-density lipoprotein cholesterol and triglyceride levels, smoking, platelet hyperactivity etc). The ultimate goal is to prevent or reduce the incidence and severity of diabetic complications. In this setting, the use of agents able to correct insulin deficiency has been proved to be effective in metabolic control.

Gliclazide modified release (MR) is a new formulation of a well known sulphonylurea which allows once-daily administration for optimal compliance. In patients with type 2 diabetes mellitus, gliclazide MR stimulates both first and second phase insulin secretion and improves insulin pulsatility. Gliclazide MR reduces both fasting and postprandial plasma glucose levels.

This new formulation in a 30mg once daily dosage has been shown in a randomised, 10-month, double-blind multicentre study to be as effective as 80 mg/day of the standard formulation in reducing glycosylated haemoglobin (HbA_{1c}) levels. A low incidence of minor hypoglycaemic episodes was observed, even in 'at-risk' groups (patients aged 65 years or more with or without renal insufficiency). A sustained metabolic effect was documented by a 12-month extension of the trial.

Gliclazide MR binds selectively to the sulphonylurea receptor SUR1 expressed on the β-cell membrane, and induces insulin secretion by closing ATP-sensitive potassium (K_{ATP}) channels. At therapeutic concentrations, it does not bind to SUR isoforms SUR2A and SUR2B expressed by cardiac and smooth muscle vascular cells, respectively. Such a specificity for β-cell receptors is absent in comparative studies performed with other sulphonylureas such as glibenclamide and glimepiride. Clinically, closing cardiac K_{ATP} channels may induce alterations in myocardial ischaemia preconditioning, as recently shown in patients treated with glibenclamide.

Finally, in addition to its metabolic effects, gliclazide MR exerts specific antioxidant properties and reverses endothelial dysfunction. These properties are of particular interest in preventing diabetic micro- and macrovascular complications. ▲