

EudraCT 2014-002685-70 (300A , The Effect of Sitagliptin on Glucagon Dynamics and Incretin Hormones During Mild Hypoglycemia in Elderly Patients with Metformin-Treated Type 2 Diabetes)

AIMS:

Maintenance of glucagon response to hypoglycaemia is important as a safeguard against hypoglycaemia during glucose-lowering therapy in type 2 diabetes. During recent years, DPP-4 (dipeptidyl peptidase-4) inhibition has become more commonly used in elderly patients. However, whether DPP-4 inhibition affects the glucagon response to hypoglycaemia in the elderly is not known and was the aim of this study.

METHODS:

In a single-centre, double-blind, randomized, placebo-controlled crossover study, 28 subjects with metformin-treated type 2 diabetes (17 male, 11 female; mean age, 74 years [range 65-86]; mean HbA1c, 51.5 mmol/mol [6.9%]) received sitagliptin (100 mg once daily) as add-on therapy or placebo for 4 weeks with a 4-week washout period in between. After each treatment period, the subjects underwent a standard breakfast test, followed by a 2-step hyperinsulinaemic hypoglycaemic clamp (target 3.5 and 3.0 mmol/L), followed by lunch.

RESULTS:

Glucagon levels after breakfast and lunch, and the glucagon response at 3.5 mmol/L, were lower after sitagliptin than after placebo. However, the glucagon response to hypoglycaemia at 3.1 mmol/L did not differ significantly between the two. Similarly, the noradrenaline, adrenaline and cortisol responses were lower with sitagliptin than with placebo at 3.5 mmol/L, but not at 3.1 mmol/L glucose. Responses in pancreatic polypeptide did not differ between the two.

CONCLUSIONS:

Elderly subjects with metformin-treated type 2 diabetes have lower glucagon levels at 3.5 mmol/L glucose, but maintain the glucagon response to hypoglycaemia at 3.1 mmol/L during DPP-4 inhibition, which safeguards against hypoglycaemia and may contribute to decreasing the risk of hypoglycaemia by DPP-4 inhibition in this age group.