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Nateglinide

A Viewpoint by Riccardo Perfetti

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The onset of type 2 diabetes is characterised by 2 determining factors: insufficient ability to secrete insulin and/or resistance to its biological action.[1] Current biomedical research continues to clarify the relative contributions of these defects to the pathogenesis of type 2 diabetes, and novel pharmacological agents are designed specifically to correct either the impaired insulin secretory activity or the resistance to the action of insulin.

A novel non-sulphonylurea insulin-secreting agent, nateglinide, appears to correct specifically postprandial hyperglycaemia, a characteristic feature of newly diagnosed type 2 diabetes. When dietary changes and physical exercise have failed to restore euglycaemia, nateglinide has the potential to be a preferred treatment for the very large population of patients with isolated postprandial hyperglycaemia but with normal fasting plasma glucose levels.

Nateglinide is a phenylalanine derivative that rapidly stimulates insulin release. In healthy volunteers, it is rapidly absorbed when administered before meals, with a peak of absorption reached within 20 minutes in 1 study.[2] The clearance of nateglinide appears equally rapid, with disappearance of half of the absorbed drug within 0.98 ± 0.06 hours in the same study.[2] In patients with diabetes, nateglinide increases plasma insulin levels within 20 to 40 minutes and promotes a hypoglycaemic effect within 30 to 90 minutes of oral administration.[2]

Nateglinide is believed to bind to the common sulphonylurea receptor of the β-cell and to exert its insulinotropic action via closure of K^+ channels.[3] Because of the rapid onset and short duration of action, the main action of nateglinide is reflected by a potentiation of the early phase of insulin release.[4,5] Unlike classic sulphonylurea drugs, nateglinide does not inhibit the counter-regulatory glucagon response to hypoglycaemia, and repeated administration for 2 weeks enhances insulin secretion in the same way as a single dose,[6] thus providing a consistent effect without the risk of hypoglycaemia. Comparison of plasma glucose profiles in individuals receiving nateglinide or other available insulinotropic agents suggests that nateglinide has the most rapid onset and shortest duration of action. This results in a more physiological mealtime insulin secretion, lower plasma insulin levels and reduced frequency of hypoglycaemic reactions.[7-9]

Because of the growth of the choice of treatments for patients with diabetes, it is imperative that physicians become familiar with new agents like nateglinide that are likely to be introduced for clinical use in the very near future. It is also important to remember that these new pharmacological agents should always be used in conjunction with dietary modification, exercise and education to ensure the best possible therapeutic outcome. ▲

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