OBSERVATIONS

Type III Allergy to Insulin Detemir

Allergy to insulin has become rare with human recombinant insulin or its analogs, with an estimated incidence of <1%. The most common clinical situation is related to the type I allergic reaction in the Gell and Coombs classification and usually consists of a local wheal-and-flare eruption at injection site with induration, pruritus, and burning sensation that appear a few minutes after the injection and last for 1–2 h; this reaction is rarely systemic, with urticaria, angioedema, or anaphylactic shock. Insulin can also be infrequently responsible for a late type III Arthus' reaction, characterized by the development of subcutaneous nodules at the injection site 2–6 h after administration (1). And last, insulin allergy may be rarely related to a type IV T-cell–mediated delayed reaction that appears 8–12 h after injection, peaks at 24 h, and lasts for several days with painful, itchy, local mononuclear infiltration.

To our knowledge, we report the first case of type III allergy to the new long-acting insulin analog detemir. A 31-year-old man with type 1 diabetes for 20 years was admitted for uncontrolled diabetes. He had no history of any allergy. He had been treated by glargine (Lantus; Sanofi-Aventis) once daily and aspart (Novorapid; Novo Nordisk) before each meal for 2 years. We decided to switch insulin glargine for detemir to optimize glycemic control. Six hours after the first injection of detemir, the patient presented a subcutaneous small, subdermal, nonpruriginous, slightly painful nonerythematous nodule with central hematoma at injection site (left arm). On the 2 following days, the same localized reaction occurred 4–6 h after the detemir injection (right arm, left thigh), although no reaction to aspart was noticed. Local factors such as poor injection technique, misuse of insulin injector, or use of impure alcohol were ruled out. Detemir was then switched back for glargine. The nodules spontaneously disappeared in ~48 h.

We did not perform skin tests because of the explicit clinical presentation of a type III allergy and because of the potential risk of serum sickness after reintroducing detemir. However, we cannot exclude that an excipient rather than insulin detemir itself could be responsible for this allergy. Nevertheless, the only additive present in detemir preparation and not in glargine or aspart preparations is mannitol, and allergy to mannitol is exceptional and related to IgE-mediated anaphylaxis (type I reaction) (2). To our knowledge, we report here the first case of allergy with insulin detemir.

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Efficacy of Pitavastatin, a New HMG-CoA Reductase Inhibitor, on Lipid and Glucose Metabolism in Patients With Type 2 Diabetes

Type 2 diabetes is one of the risk factors for macrovascular disease. Treatment of hypercholesterolemia is important in patients with type 2 diabetes to prevent macrovascular disease. The 3-hydroxy-3-methyl glutaryl-coenzyme A (HMG-CoA) reductase inhibitors (statins) are key drugs to lower the cholesterol level not only in nondiabetic patients but also in patients with type 2 diabetes. However, some statins might worsen glycemic control (1) whereas some of them might be neutral (2) or improve glycemic control (3), and their effects on glucose metabolism are controversial. Pitavastatin, an HMG-CoA reductase inhibitor, has been available in Japan since 2003 (4) and the Republic of Korea since 2005, and its effect on glucose metabolism in diabetic patients remains unknown. Since safe use of statins is important for patients, we evaluated the effects of pitavastatin on lipid and glucose metabolism in this study.

A total of 79 type 2 diabetic patients (47 men and 32 women; mean age ± SD 61.7 ± 12.1 years; BMI 26.7 ± 4.2 kg/m^2) with hypercholesterolemia who had never been treated with statins and attended one of five outpatient diabetic clinics were enrolled. Informed consent was obtained from all subjects. This study was designed as an 8-week intervention period with new administration of pitavastatin (1 or 2 mg/day). Fasting plasma glucose, HbA_{1c}, LDL cholesterol, HDL cholesterol, triglycerides, aspartate aminotransferase, alanine aminotransferase, γ-glutamyl-transferase, and creatine phosphokinase levels were measured both before and after 8 weeks of pitavastatin treatment. Differences in these parameters pre- and posttreatment were analyzed using Wilcoxon's matched-pair signed-rank test.

Pitavastatin treatment resulted in a significant decrease in LDL cholesterol levels (from 4.28 ± 0.69 to 2.70 ± 1.03 mmol/l, $P < 0.0001$) and triglyceride levels (from 1.71 ± 0.76 to 1.54 ± 1.09 mmol/l, $P < 0.0001$), whereas the change in HDL cholesterol levels did not reach statistical significance (from 1.29 ± 0.32 to 1.33 ± 0.33 mmol/l, $P = 0.055$). Concerning glycemic control, changes in fasting plasma glucose levels (from 8.20 ± 2.71 to 8.27 ± 2.10 mmol/l) and HbA_{1c} levels (from 7.25 ± 1.60 to 7.27 ± 1.47%) were not statistically significant. Changes in other available parameters were also not statistically significant. No subject terminated the trial because of adverse events.

Our results showed that pitavastatin is a potent agent for lowering LDL cholesterol level and that it does not affect glycemic control in patients with diabetes. Although statins have been widely prescribed all over the world and are regarded as the first choice for hypercholesterolemia, physicians must pay attention to the adverse effects of these agents, e.g., myotoxicity, liver dysfunc-

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