A Case of Lipoatrophy With Insulin Glargine

Long-acting insulin analogs are not exempt from this complication

Lipoatrophy as a cutaneous complication of insulin therapy became extremely rare since the introduction of recombinant human insulin. Recently, some cases of lipoatrophy were reported in association with the use of rapid-acting insulin analogs, like lispro insulin, in combination with pump therapy (1, 2). If long-acting insulin analogs are exempt from this complication, the complications are not known.

We report the case of a 39-year-old type 1 diabetic Caucasian woman (weight 50 kg, BMI 21.4 kg/m²) with diabetes duration of 8 years. She began intensified insulin therapy with two premixed insulin injections before breakfast and dinner and regular insulin before lunch (20 IU/day, 72% neutral protamine Hagedorn insulin). In January 2004, she agreed to participate in a 6-month randomized study comparing different multiple daily insulin therapies, all using bedtime insulin glargine as basal insulin. No specific instructions about the preferred injection area for both insulins were given, but it is a common practice in our country to inject rapid-acting insulin into the abdomen and long-acting insulin into the buttock or thigh.

At follow-up, a lipoatrophic area appeared at study end in the outside, upper third of the right thigh (Fig. 1). Asking the patient about the possible causes, she recognized that she didn’t change pen needles frequently and, even more importantly, she had used the right thigh for glargine injection almost exclusively. She was prompted to avoid the right thigh for insulin injection shifting to buttock or left thigh areas and changing the area every day. However, 12 months later the lipoatrophy area persisted with the same extent.

This case confirms that any insulin preparation, even insulin analogs, may induce lipoatrophy. Insulin glargine, a diargynil insulin analog, is a new long-acting insulin analog soluble at acid pH (4.0) but less soluble at neutral pH because its isoelectric point is at a pH level of ~6.4–6.6. After subcutaneous injection, precipitation or crystallization of glargine at the site of injection delays absorption and prolongs the effect of insulin, allowing a peakless, nearly 24-h duration of action (3).

Insulin glargine is now being used extensively as basal insulin in both type 1 and type 2 diabetes. To our knowledge, this is the first description of lipoatrophy induced by insulin glargine. Certainly, the frequent use (up to 14 times) of the same pen needle and the repeated injection into the same area were relevant to the appearance of lipoatrophy in this case. Under such circumstances, we did not know if in this case the injection of an acid insulin solution and the subsequent formation of crystals in the subcutaneous tissue could have played a role in lipoatrophy formation. It has been suggested earlier that lipoatrophy results from a local immune reaction to insulin crystals (4). The inflammatory response includes local hyperproduction of tumor necrosis factor α from macrophages that led to dedifferentiation of adipocytes (lipoblastoma-like lipoatrophy) (4).

In conclusion, daily pen needle change and frequent switching of injection area are even more important with insulin glargine to avoid lipoatrophy.

F. JAVIER AMPUDIA-BLASCO, MD1
JUAN GIRBES, MD2
RAFAEL CARMENA, MD3

From the 1Diabetes Reference Unit, Endocrinology Department, Clinico University Hospital València, Spain; and the 2Diabetes Unit, Arnau de Vilanova Hospital, Valencia, Spain.

Address correspondence to Dr. F. Javier Ampudia-Blasco, Diabetes Reference Unit, Endocrinology Department, Clinico University Hospital València, Avda Blasco Ibáñez, 17, 46010 Valencia, Spain. E-mail: francisco.j.ampudia@uv.es.

© 2005 by the American Diabetes Association.

References

A Comparison of Lipid and Glycemic Effects of Pioglitazone and Rosiglitazone in Patients With Type 2 Diabetes and Dyslipidemia

Response to Goldberg et al.

The study by Goldberg et al. (1) in the July issue of Diabetes Care concluded that, compared with rosiglitazone, pioglitazone was associated with improvements in triglycerides, HDL cholesterol, LDL concentration, and LDL particle size. It should first be noted that 4,410 subjects were screened to obtain 735 eligible subjects. This was a highly selective

COMMENTs and RESPONSEs
group, and therefore this was an enriched study. Second, recognized goals for the diabetic patient were not reached with either pioglitazone or rosiglitazone for triglycerides, non-HDL cholesterol, and LDL cholesterol. Third, HDL particle size, which should have been available from the proton nuclear magnetic resonance spectroscopy of Liposcience, was not reported. Why was this omitted from both the American Heart Association presentation and the Diabetes Care study?

Finally, and most importantly, based on the Collaborative Atorvastatin Diabetes and Heart Protection Studies (2,3), it is now well recognized that irrespective of LDL levels, all type 2 diabetic patients benefit from statin therapy. Without concomitant statin therapy, these results have little clinical significance. This is especially important since two studies have clearly shown that when simvastatin or ezetimibe are coadministered with thiazolidinediones there are no significant differences in the lipid profile of those subjects on pioglitazone or rosiglitazone (4,5).

It is now clear for many studies that rosiglitazone does not decrease fasting triglycerides. However, two recent studies have shown that rosiglitazone does significantly decrease postprandial triglycerides. One study has shown that pioglitazone does not decrease postprandial triglycerides when added to thiazolidinedione therapy in patients with type 2 diabetes mellitus: a multicenter, randomized double blind placebo controlled trial. Lancet 361:685–696, 2004


A Comparison of Lipid and Glycemic Effects of Pioglitazone and Rosiglitazone in Patients With Type 2 Diabetes and Dyslipidemia

Response to Goldberg et al.

Goldberg et al. (1) report a randomized comparison of the effects of two thiazolidinediones (TZDs), pioglitazone (Actos) and rosiglitazone (Avandia), on lipid and lipoprotein levels in individuals with diabetes treated with diet and/or oral monotherapy. Many changes in these lipids and lipoproteins seemed to be in favor of pioglitazone. Two important pieces of information were not included in the published study.

First, ~80% of subjects were termed completers. Completers were defined as those who had at least one blood sample drawn on a TZD. If they quit the study, this last observation was carried forward for final analysis. It is possible that a number of subjects dropped out while on the initial dose of the respective TZD and this would enrich the population with those on pioglitazone rather than rosiglitazone.

Second, what were HDL subfraction responses as determined by nuclear magnetic resonance? Was there a similar response of big, intermediate, and small HDL particles? Some of the lipoprotein and lipid changes seen with pioglitazone appear to be those that would be expected as a peroxisome proliferator–activated receptor-α effect. What was the response of big and intermediate size HDL, those that are antiatherogenic (2), and the small HDL that is less antiatherogenic?

John D. Brunzell, MD

From the Division of Metabolism, Endocrinology and Nutrition, University of Washington, Seattle, Washington.

Address correspondence to John D. Brunzell, Professor of Medicine, Division of Metabolism, Endocrinology and Nutrition, University of Washington, 1959 NE Pacific St., Box 356426, Seattle, WA 98195-6426. E-mail: brunzell@u.washington.edu

D.B. has been a member of advisory boards for and has received consulting fees from GlaxoSmithKline, Novartis, Sanofi-Aventis, and Ligand Pharm. © 2005 by the American Diabetes Association.

References


2. Cameron JM, Friberg P, Rafferty PA, Mavromaras K, O’Donnell MG, Oliver RT, the GLAI Study Investigators: Comparison of the effects of pioglitazone and rosiglitazone on lipid and glycemic effects of pioglitazone in patients with type 2 dia-

