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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, 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/m^2) 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 diarginyl insulin analog, is a new long-acting insulin analog soluble at acid pH (4.0) but less soluble at neutral pH because

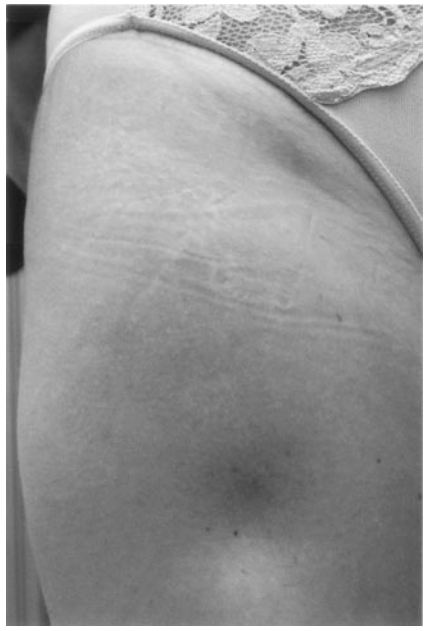

Figure 1—*Lipoatrophic area on the outside, upper part of thigh where insulin glargine was injected.*

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 dedifferention 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, MD[1]
Juan Girbes, MD[2]
Rafael Carmena, MD[1]

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

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

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COMMENTS AND RESPONSES

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