

patients with AD have been found to have increased IgE levels and high-affinity receptors for IgE [1] it can be assumed that treatment with an anti-IgE antibody may decrease clinical manifestations and disease activity.

To test this hypothesis, we conducted a study in patients with a diagnosis of severe AD (SCORAD score >50 points) from the allergy service at Hospital Adolfo López Mateos in Mexico City, Mexico over a period of 10 months. A complete clinical history was taken and laboratory tests, including IgE, were requested. Omalizumab treatment was started with doses adjusted to weight and IgE levels. Patients were periodically evaluated, with physical examination and assessment of SCORAD score, use of drugs, presence of adverse effects, and quality of life using the Dermatology Life Quality Index (DLQI) [6].

The software program SPSS 15.0 for Windows was used for statistical analyses.

Eleven patients (1 male and 10 females) aged between 12 and 52 years with severe AD were enrolled.

The baseline SCORAD score ranged from 43 to 101 points, with a mean of 71.2 points. A gradual improvement was seen in all patients, with a mean of 31.54 points after 10 months ( $P<.05$ ). Mean (SD) quality-of-life scores also improved, from 9.36 points to 3.72 (1.48) over the same period ( $P<.05$ )

There have been previous reports of AD treated with omalizumab. Vigo [7] reported a significant improvement in the symptoms of all 7 patients treated, and Belloni et al [8] reported a favorable response in 6 of 11 patients. Krathen and Hsu [9], however, observed no response to omalizumab in 3 patients with severe AD.

In our patients, there was a gradual improvement in SCORAD scores, accompanied by a decrease in symptoms and an improvement in quality of life, with fewer limitations in terms of attendance at school, work, etc. No adverse effects were observed.

The limitations of this study are the small sample size and the lack of comparison with a placebo group.

Omalizumab treatment progressively decreased the severity of AD, evaluated by SCORAD, with a gradual decrease in symptom intensity, which was reflected by improved quality-of-life scores.

It is necessary to conduct studies with more patients and, if similar results to the ones presented here are found, omalizumab may become a first-line therapy, capable of achieving good disease control and preventing complications in the treatment of moderate and severe AD.

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## A Severe Case of Lipoatrophy Due to Human Insulin and Insulin Analogs in a Patient With Diabetes: Is an Immunological Mechanism involved?

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Palabras clave: Diabetes. Insulinas. Lipoatrofia. Hipersensibilidad tipo III.

Although there have been few reports of lipoatrophy as a cutaneous side effect of recombinant human insulin or insulin analogues, in recent years, there have been an increasing number of case reports and letters in the scientific literature indicating that lipoatrophy may also develop after treatment with these insulins [1-5]. Immunological mechanisms have been proposed, but the exact pathogenesis of lipoatrophy remains obscure [6].

Table. Specific Immunoglobulin (Ig) G and IgG4 Subclass Values and Precipitin Study Results

	Patient		Control		Patient	Control 1	Control 2
	IgG, mg/mL	IgG4, mg/mL	IgG, mg/mL	IgG4, mg/mL			
Apidra	2.84	0.06	0	0	(-)	ND	ND
Humalog	2.73	0.04	0	0	(-)	ND	ND
Novorapid	2.59	0.05	0	0	(-)	ND	ND
Actrapid	2.62	0.01	0	0	(+)	(-)	(-)
Insulatard	6.94	0.02	0	0	(+)	(-)	(-)
Levemir	3.38	0.08	0	0	(+)	(-)	(-)
Lantus	45.3	0.02	27.4	0	(+)	(-)	(-)
Protamine	3.44	0.05	0	0	(+)	(-)	(-)

Abbreviations: ND, not done.

A 30-year-old woman, diagnosed 2 years previously with type 1 diabetes mellitus and primary autoimmune hypothyroidism, had experienced a severe depression of the skin surface consistent with lipoatrophy over the past year; the depression affected the sites where she administered subcutaneous insulin. During this time, she had used different types of insulins, including short-acting insulin (insulin glulisine [Apidra]), insulin lispro [Humalog], insulin aspart [Novorapid]; long-acting insulin (insulin detemir [Levemir] and insulin glargine [Lantus]); and premixed insulin (insulin-aspart + isophane insulin [Novomix]). She did not relate the lipoatrophic areas with the administration of a specific insulin.

Skin biopsy of the lipoatrophic areas and immunofluorescence against immunoglobulins, complement fractions, and fibrinogen were performed. Skin prick, intradermal, and patch tests were performed with all the insulins she had been using as well as with human insulin (Actrapid), isophane insulin (Insulatard), and protamine. The results were read at 20 minutes and at 48 and 96 hours. Specific immunoglobulin (Ig) G and IgG4 subclass were measured by biotinylation using ImmunoCAP (Phadia, Uppsala, Sweden) and precipitins against human insulin, protamine, and all the insulins mentioned above were determined by the Ouchterlony technique. Specific IgE against human insulin and protamine were also measured.

In vivo skin tests (prick, intradermal, and patch tests) and specific IgE against human insulin and protamine were negative (<0.35kU/L). High levels of IgG and IgG4 were observed for all the insulins tested as well as for protamine, with higher levels noted for medium- (Insulatard) and long-acting insulins (Levemir and Lantus) than for short-acting insulins (Table). As a control for the IgG and IgG4 determinations, a mixed pool of neonatal sera was used, with negative results for all the insulins tested, except for Lantus, which yielded high IgG levels. The precipitin study was positive for Actrapid, Insulatard, Levemir, Lantus, and protamine and negative for Apidra, Humalog, and Novorapid (Table). Two patients with diabetes who had used these insulins in the past served as controls and showed negative precipitins against all the insulins tested. The skin biopsy showed lipoatrophy, with some areas of inflammatory neutrophilic infiltrate but no signs of

immunoglobulins, complement factors, or fibrinogen deposits in the immunofluorescence study.

The positive IgG result for 1 insulin in the control sera rendered this measurement useless, and it was therefore decided to select an alternative insulin based on the results of the precipitin study. All the long-acting insulins tested had yielded positive results in this study and therefore, after consultation with the patient, it was decided to start continuous subcutaneous insulin infusion with insulin glulisine (Apidra), for which the precipitin study had been negative. After 6 months, the lipoatrophic areas improved significantly and no new skin lesions were observed.

We have presented a case of severe lipoatrophy in a patient with diabetes. A type III hypersensitivity reaction could explain the symptoms because of the detection of precipitins to insulins used by the patient. On the other hand, the lack of an abnormal deposit of immunological components does not support this hypothesis but, as the biopsied area corresponded to an old lesion, the immunological deposits might have been eliminated over time. The excipients of all the insulins were tested and no correlation was observed with the results obtained. Although the frequency of this cutaneous complication of insulin therapy has decreased since the introduction of various short- and long-acting insulin analogues, lipoatrophy can also develop after treatment with these compounds.

The precipitin technique has been used in insulin resistance and immunity studies since the 1940s [7]. In the case described, the technique proved, once again, to be a valid method for choosing the most appropriate insulin. However, whether or not an immunological mechanism was involved in the lipoatrophic process remains uncertain, and further studies with adequate immunological assessment are necessary.

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## Fixed Drug Eruption Due to Meloxicam

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**Key words:** Meloxicam. Fixed drug eruption. Oxicam. Cross-reaction. Patch tests.

**Palabras clave:** Meloxicam. Erupción fija medicamentosa. Oxicam. Reactividad cruzada. Pruebas epicutáneas.

Fixed drug eruption (FDE) is a common cutaneous adverse drug reaction involving a delayed T-cell hypersensitivity reaction [1]. The most characteristic finding of FDE is recurrence of similar lesions at the same sites and healing with residual hyperpigmentation [2]. FDE appears within minutes to several hours after intake [1]. Rechallenge is the most reliable method of identifying causative drugs, but application of patch tests, especially in the affected area, has gained the most attention to date [1]. Nonsteroidal anti-inflammatory drugs (NSAID) are one of the principal causes of FDE [3]. Although a few cases of piroxicam-induced FDE have been reported [4-7], FDE caused by oxicams is rare. We report an unusual case of FDE due to meloxicam. To the best of our knowledge, this is the first report of FDE due to meloxicam.

A 44-year-old woman with rheumatic disease was referred to our clinic for assessment of several episodes of cutaneous eruption after ingestion of analgesics. She had

a history of brownish, sharply demarcated, round pruritic plaques suggestive of FDE on the right knee and forearm with concomitant vulvar pruritus 10-15 minutes after oral intake of flurbiprofen, ibuprofen, and piroxicam. The last reaction occurred 4 years ago. At presentation, the patient had no residual lesion. Because of her underlying rheumatic disease, she needed a safe NSAID. Considering the safety profile of meloxicam in patients with aspirin-exacerbated respiratory diseases (AERD) and aspirin-induced urticaria [8,9], we performed a single-blind placebo-controlled oral challenge test with increasing doses of meloxicam up to a cumulative dose of 7.5 mg. No reaction occurred with the placebo. However, 45 minutes after ingestion of meloxicam, the patient reported vulvar pruritus, and a brownish pruritic plaque appeared on the right knee (Figure). The reaction responded well to a topical corticosteroid. Four weeks later, cross-reactivity within the group was analyzed using patch tests with 0.1% piroxicam, 1% piroxicam, 1% tenoxicam, 1% meloxicam, and 10% nimesulide, all in white petrolatum, on both the previously affected area (right knee) and unaffected skin (back). Only 1% piroxicam on previously affected skin was positive at 72 hours, and the results of the remaining patch tests with oxicams and nimesulide were negative. Subsequently, oral challenge tests with nimesulide and naproxen were performed, and both were negative.



Figure. Brownish plaque that appeared on the right knee 45 minutes after ingestion of a cumulative dose of 7.5 mg of meloxicam.