



Letter

Omalizumab in the treatment of antihistamine-resistant chronic urticaria in adults

Chronic urticaria is characterized by hives and/or angioedema that occurs for more than 6 weeks at a time.¹ Although the use of high doses of second-generation histamine₁ antihistamines has recently been proposed as a treatment for this condition, biological therapy against IgE has also emerged as a new alternative for the treatment of chronic spontaneous urticaria.^{2–6}

This study assessed the effectiveness of omalizumab to treat spontaneous or inducible urticaria in the Mexican population. The ethics and research committees of the Hospital Regional “Lic. Adolfo López Mateos,” Instituto de Seguridad y Servicio Sociales de los Trabajadores del Estado approved our study, and each patient provided written informed consent to participate. When building our cohort, we included patients 18 years or older who had inducible or spontaneous chronic urticaria and those who had a refractory response to antihistamines at a standard dose after 2 weeks, as defined by a Urticaria Activity Score 7 (UAS-7) score of 16 points or more. We excluded all patients with a history of asthma or allergic rhinitis, anaphylactic reactions or hypersensitivity to omalizumab, neoplasms, greater than 10% weight loss in the 6-month period before the study, and autoimmune disease, women who were pregnant or breastfeeding, and patients using systemic or topical corticosteroids. Consecutive patients were recruited by nonprobability sampling from March 1, 2014, through February 29, 2015. All the patients in our study were initially treated with 5 mg/d of levocetirizine for 2 weeks to control urticaria (157 patients). The 82 patients who responded to the treatment were excluded. The 76 patients who continued to have chronic urticaria with a UAS-7 score greater than 16 points went to a second phase of treatment with 20 mg/d of levocetirizine (4 times the common dose) for 4 weeks. Patients who achieved control of urticaria with this dose (50 patients) did not participate in the final stage. Patients who did not achieve control or had inadequate control of their urticaria (26 patients) continued to the third stage in which omalizumab was administered subcutaneously at a set dosage of 300 mg every 4 weeks. The clinical follow-up was performed monthly using the UAS-7 and Urticaria Control Test (UCT).⁷

Slightly more than 70% of the patients had spontaneous chronic urticaria, and almost one-third had inducible urticaria (Table 1). Patients with chronic urticaria who were being treated with omalizumab had a baseline median UAS-7 score of 32 points, which became significantly lower after the first month ($P < .001$) and remained so until the sixth month of treatment. When the study was completed, no patients had a complete response, and 26 patients manifested a UAS-7 score of 6 or less. Patient control of urticaria, as measured by the UCT, revealed a significant increase in the median score, ranging from 6 to 13 points ($P < .001$). This improvement was consistent for 4 weeks after the first dose of omalizumab, and notably, there was progress until the sixth month.

According to the UCT, 2 of 26 patients (7.7%) were considered to have poor control of their urticaria. The adverse effect frequency for omalizumab was 7.7% ($n = 2/26$). Headaches were the most adverse side effect; however, treatment was not discontinued.

This study found that a subcutaneous dosage of 300 mg of omalizumab, when given every 4 weeks, is highly effective and safe. Different treatment options using omalizumab have been tested in chronic urticaria.^{2,3,5} Doses of 300 mg per month are more effective in treating urticaria that is resistant to antihistamines or anti-leukotrienes² and reducing the UAS-7 score, as well as the acute-ness score of itching.⁵ In real-life scenarios, some studies have found that 150 or 300 mg of omalizumab resulted in complete remission in 69% to 86%,^{8,9} surpassing cyclosporine in symptom remission and improvement in quality of life.³ In our cohort, administering 300 mg of omalizumab every 4 weeks allowed most patients to have good control of urticaria (UAS-7 score ≤ 6), which is markedly different from previous studies in which 37% to 51% of patients achieved high control.^{2,6}

Urticaria is an illness that is primarily induced by the activity of mastocytes; however, all the signals that stimulate its activation have not yet been properly defined.¹ Omalizumab appears to have direct activity on mast cells and basophils.³ Notably, patients who were eligible to receive omalizumab had significantly higher concentrations of basophils and lower eosinophil counts than those who received high doses of levocetirizine. Patients with chronic urticaria tend to have a higher frequency of basopenia¹⁰; however, in our study, this phenomenon was not observed among patients who received omalizumab. This finding suggests that an elevated basophil count in peripheral blood could be indicative of the type of patient who would benefit from omalizumab use. In terms of the differences in eosinophil counts among groups, it has been suggested that the main protein of these cells could activate basophils.¹⁰ To date, we are unaware of the real meaning behind such an occurrence.

A recent study⁶ has documented 2 categories of responses to omalizumab: an early response (before 4 weeks) and a latent response (after 3 months). In this cohort, most of the patients showed improvement within the first month; however, the mechanisms that explain this behavior have not been described to date.⁴

The duration of symptom suppression in patients who have received a dose of omalizumab is still being researched. Moreover, if the use of omalizumab is discontinued, symptoms do not return to their original severity. It appears that the underlying process of urticaria is not modified by the use of omalizumab.^{4,6,11}

Our results, obtained from clinical scenarios, support the recommendations provided by international associations¹ regarding the use of omalizumab as a treatment option for spontaneous urticaria.

Table 1
Characteristics of the study population^a

Characteristic	Total sample (N = 76)	Levocetirizine (n = 50)	Omalizumab (n = 26)	P value
Female	61 (80.3)	40 (80)	21 (80.8)	.94
Age, mean (SD), y	47.9 (12.5)	46.9 (13.8)	50.1 (9.3)	.28
Type of urticaria				.18
Spontaneous	54 (71.1)	33 (66.0)	21 (80.8)	
Inducible	22 (28.9)	17 (34.0)	5 (19.2)	
Presence of angioedema	44 (57.9)	25 (50.9)	19 (73.1)	.053
Evolution of urticaria, mean (SD), y	4.7 (1.3)	4.5 (1.3)	5.0 (1.3)	.13
Total serum IgE (IU/mL), median (IQR)	69.2 (30.2–165.2)	72.5 (21.3–138.5)	55.5 (31.5–186.0)	.91
Total eosinophils, median (IQR), $\times 10^3/\mu\text{L}$	0.170 (0.100–0.300)	0.190 (0.100–0.310)	0.131 (0.049–0.182)	.02
Total basophils, median (IQR), $\times 10^3/\mu\text{L}$	0.010 (0.005–0.020)	0.010 (0.004–0.016)	0.020 (0.010–0.022)	.01
Autologous serum positive test result	35 (46.1)	19 (38.0)	16 (61.5)	.051

Abbreviation: IQR, interquartile range.

^aData are presented as number (percentage) of patients unless otherwise indicated.

There are several limitations in the study regarding sample size, lack of a comparison group (instead, an intragroup comparison was conducted: before and after), lack of quality of life indicators showing how each patient is affected by his/her condition, and the absence of follow-up of patients after discontinuation of the biological treatment.

In conclusion, in clinical scenarios, the use of subcutaneous omalizumab at a set dose of 300 mg for a period of 6 months was an effective and fast-acting therapeutic option to treat spontaneous urticaria in patients who do not respond to antihistamines.

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