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A randomized, double-blind, active-controlled, parallel-group pilot study to compare the efficacy and sedative effects of desloratadine 5 mg with levocetirizine 5 mg in the treatment of chronic idiopathic urticaria

To the Editor: The new generation antihistamines, such as desloratadine and levocetirizine, have provided major advances in the treatment of chronic idiopathic urticaria (CIU).¹ There has been debate regarding the efficacy and sedative effects of desloratadine and levocetirizine, with findings from several studies indicating that levocetirizine is superior to desloratadine in terms of drug activity.^{2,3} However, the comparative sedative effects of the two drugs have not been well studied.

We conducted a randomized, double-blind, active-controlled, parallel-group pilot trial of 64 patients (20 males, 44 females) with CIU who received once-daily desloratadine 5 mg (Denosin; Lotus Pharmaceutical, Taipei, Taiwan) and levocetirizine 5 mg (Xyzal; UCB

Farchim SA, Switzerland) for 6 weeks (Fig 1). The therapeutic response to the study medication, jointly assessed by the investigator and the patients, was evaluated every 2 weeks using a 5-point scale (1 = complete relief, 2 = marked relief, 3 = moderate relief, 4 = slight relief, and 5 = treatment failure). Sedative effects were assessed using the Epworth Sleepiness Scale (ESS), visual analogue scale (VAS), and Stanford Sleepiness Scale (SSS). Data pertaining to efficacy and sleepiness were compared between treatment groups by fitting marginal linear regression models using the generalized estimating equations method for our repeated measures data, with treatment and baseline values included in the model.⁴

In the multivariate analysis, we found that conditioning on age, gender, body mass index, renal/liver function, health problems, interactions between visits and treatments, drug changes, comedication, and completeness of treatment, levocetirizine was independently associated with a better therapeutic response than desloratadine ($P = .0468$; Table I). Levocetirizine was associated with a significantly higher VAS sleepiness score than desloratadine in the first 2 weeks of treatment ($P = .0456$; Table I) but not beyond. For ESS and SSS scores, levocetirizine was also associated with more sedative effects than desloratadine but there was no significant between-group difference.

To date, no prospective randomized study has compared levels of sedation caused by these two drugs. In 2006, a retrospective comparison of selected events from previous prescription-event monitoring studies pertaining to desloratadine and levocetirizine was conducted.⁵ It showed that levocetirizine was more likely to cause sedation than desloratadine during the first month of observation, although the overall incidence was low for both drugs. This finding is similar to that reported herein. In our study, the levocetirizine group had a higher VAS score, implying more sedation, than the desloratadine group. The between-group difference achieved statistical significance in the evaluation on day 14 but not beyond.

These results indicate that desloratadine was less sedative and levocetirizine was more efficacious. With continued treatment for more than 2 weeks, these differences in sedative effect may be somewhat minimized. The findings suggest that levocetirizine may facilitate better control than desloratadine for severe CIU. However, desloratadine should be considered if the patient has a strict contraindication to the sedative effects of levocetirizine and other antihistamines, especially in the early phase of treatment.

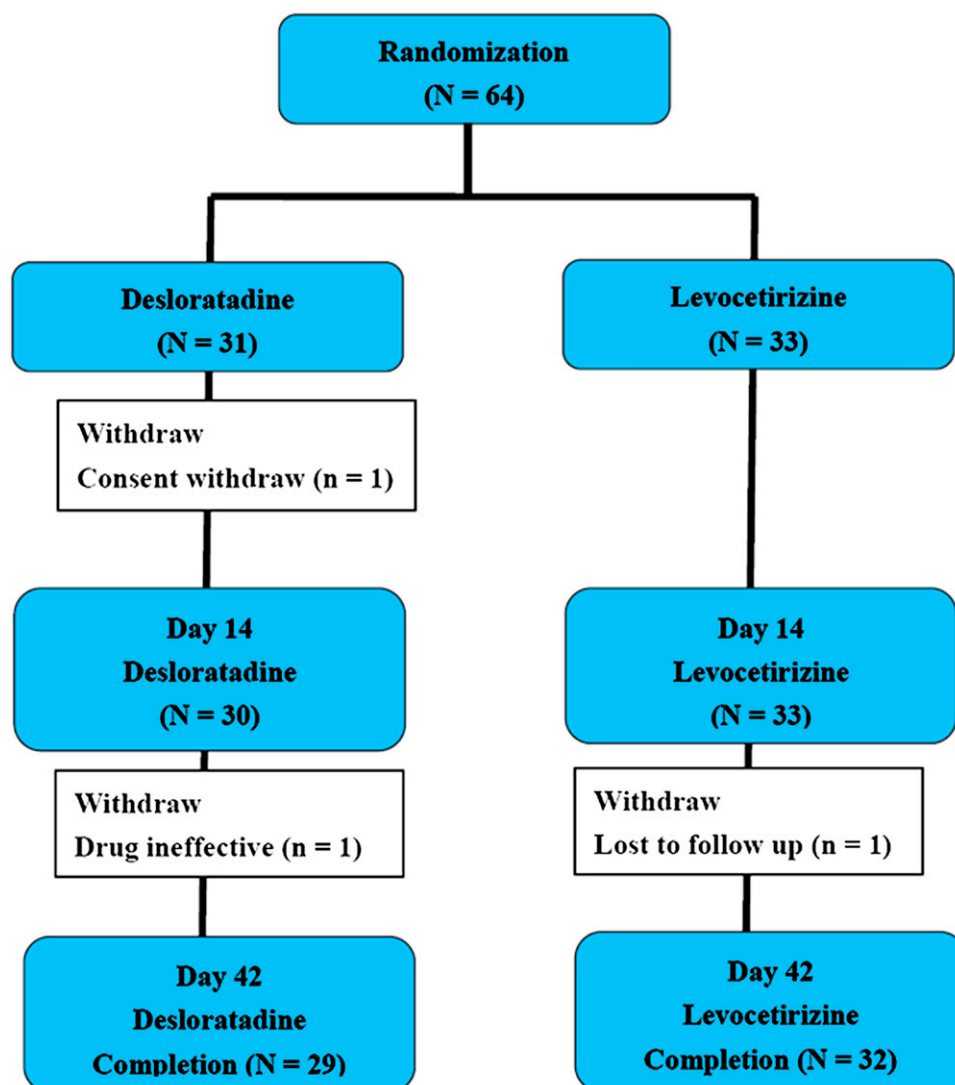


Fig 1. Flow diagram of the randomized clinical trial.

Table I. Fitted marginal linear regression models for the repeatedly measured joint therapeutic response, and VAS using the GEE method*

Covariate	Estimate	SE	95% CI	Z test	P > Z
Joint therapeutic response [†]					
Intercept	2.6985	0.1458	2.4127-2.9842	18.51	<.0001
Levocetirizine	−0.4057	0.2040	−0.8055 - −0.0058	−1.99	.0468
Visual analogue scale [†]					
Intercept	20.9444	7.1826	6.8667-35.0221	2.92	.0035
Baseline VAS score	0.6506	0.0994	0.4557-0.8454	6.54	<.0001
Age (y)	−0.3589	0.1857	−0.7228-0.0051	−1.93	.0533
Day 14 × levocetirizine [‡]	5.5035	2.7525	0.1088-10.8982	2.00	.0456

CI, Confidence interval; GEE, generalized estimating equations; SE, standard error; VAS, visual analogue scale.

*In this GEE analysis, the first-order autocorrelation (ie, AR (1)) structure fitted the repeated measures data well so that the model-based estimates of the standard errors for the estimated regression coefficients were used and reported.

[†]The values of the coefficient of determination (R^2) for these fitted marginal linear regression models were $R^2 = 0.0388$ for joint therapeutic response (number of used observations = 181), and $R^2 = 0.3544$ for VAS (number of used observations = 181), respectively.

[‡]The symbol × denotes the interaction between two covariates and can be interpreted as “and” for easy understanding.

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CASE LETTER

Imatinib treatment of generalized localized scleroderma (morphea)

To the Editor: Localized scleroderma is a chronic disease of unknown etiology that is comprised of a group of distinct conditions that involve the skin and subcutaneous tissues without internal organ manifestations. One of the more severe forms of localized scleroderma is generalized morphea, which is characterized by widespread skin involvement with multiple indurated plaques and hyperpigmentation.¹

The pathogenesis of localized scleroderma is still unclear. As in the systemic forms, transforming growth factor beta (TGF- β) and platelet-derived growth factor (PDGF) seem to play a major role in the modulation of the immune response and the regulation of extensive fibrotic processes.²

Imatinib (Glivec; Novartis, Basel, Switzerland) is a tyrosine kinase inhibitor and interferes with both TGF- β and PDGF signaling pathways by blocking the activity of c-Abl, c-Kit, and PDGF receptors, respectively.³ Concomitant side effects, such as nausea, edema, rash, and musculoskeletal pain, are relatively mild and therefore mostly well tolerated. Severe congestive cardiac failure is one uncommon side effect.

We describe the first case report of a patient with therapy resistant generalized morphea who responded to imatinib-mesylate treatment with improvement of his skin manifestations. A 74-year-old man had a 12-month history of skin hardening with

multiple large, hyperpigmented, ivory-colored indurated plaques symmetrically distributed on the trunk and the extremities. His fist closure and ankle mobility were restricted. Testing for antinuclear antibodies and Raynaud phenomenon was negative. Several treatment modalities, including psoralen plus ultraviolet A light phototherapy, cyclosporine (an initial dose of 100 mg/day up to a daily dose of 200 mg), glucocorticoids, and azathioprine had shown no effect.

We initiated off-label treatment with imatinib 200 mg per day for 6 months. Within 3 months, his skin score stabilized with a marked improvement of dermatogenous contractures (Fig 1). Twenty-Mhz ultrasound scan showed a reduction of inflammatory edema and thickness of the dermis, localized at the extensor side of the right forearm (4492 μ m vs 2297 μ m; Fig 2). Inflammatory erythematous lesions changed into hyperpigmented patches without spreading. After 6 months, we discontinued imatinib; 6 months after discontinuation, new inflammatory lesions appeared.

This case report is, to our knowledge, the first description of imatinib administration for the treatment of a patient with localized scleroderma. Our treatment with imatinib-mesylate resulted in relatively rapid and steady improvement in skin thickening. The clinical activity of the disease seemed to remain stable on the therapy, mirrored by the results