

Randomized placebo-controlled trial comparing desloratadine and montelukast in monotherapy and desloratadine plus montelukast in combined therapy for chronic idiopathic urticaria

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Background: H₁-receptor antagonists are considered to be particularly effective in reducing pruritus, and they are therefore recommended as first-line treatment in patients with chronic idiopathic urticaria (CIU). Recently, antileukotriene receptors have been used in patients with CIU, either administered as monotherapy or combined with H₁-receptor antagonists.

Objective: We compared the clinical efficacy of 5 mg of desloratadine administered once daily either as monotherapy or combined with a leukotriene antagonist, 10 mg of montelukast daily, and 10 mg of montelukast administered daily as monotherapy for the treatment of patients affected by CIU with placebo.

Methods: One hundred sixty patients aged 18 to 69 years (mean \pm SD, 43.9 \pm 13.4 years) with a history of moderate CIU were selected. A randomized, double-blind, double-dummy, placebo-controlled, parallel-group study design was used. Patients were treated with 5 mg of desloratadine once daily (n = 40), 10 mg of montelukast once daily (n = 40), 5 mg of desloratadine (n = 40) in the morning plus montelukast in the evening, or matched placebo (n = 40). Assessment of treatment efficacy was based on scores of daily cutaneous symptoms evaluated reflectively and instantaneously.

Results: Only the group treated with desloratadine as monotherapy or as combined therapy concluded the whole study. Twenty-seven of the 40 patients in the montelukast group and 35 of the 40 patients in the placebo group discontinued the treatment. As reflective evaluation, all groups showed significant differences compared with the placebo group in terms of total symptom score, number of hives, and size of largest hive. In addition to the pruritus, only the groups treated with desloratadine as monotherapy or combined therapy showed significant differences compared with those receiving

placebo, whereas there were no differences between the montelukast and placebo groups. Finally, no differences were found between the desloratadine group and the desloratadine plus montelukast group. The instantaneous evaluation demonstrated similar results regarding the desloratadine group and the desloratadine plus montelukast group versus the placebo group, whereas there were no significant differences between the group treated with montelukast alone and the placebo group for pruritus and size of largest hive. No differences were found between the group treated with desloratadine alone and the desloratadine plus montelukast group.

Conclusions: The results of this comparative study demonstrate that desloratadine is highly effective for the treatment of patients affected by CIU. In addition, the regular combined therapy of desloratadine plus montelukast does not seem to offer a substantial advantage with respect to desloratadine as monotherapy in patients affected by moderate CIU. (J Allergy Clin Immunol 2004;114:619-25.)

Key words: Chronic idiopathic urticaria, desloratadine, montelukast

Urticarial episodes lasting longer than 6 weeks are considered chronic.^{1,2} In many patients the cause of chronic urticaria (CU) cannot be identified. In such cases urticaria is defined as chronic idiopathic urticaria (CIU).^{1,2} The histopathology of CIU and the cutaneous late-phase reaction to allergen are greatly similar.³ In patients with CIU, mast cells are activated, and local tissue inflammation (pruritus and swelling) is due to histamine release and possibly other mediators, such as leukotrienes. H₁-receptor antagonists are the first-choice treatment for patients with CIU,¹ but unfortunately, some patients do not benefit from these agents.^{1,2,4-8} Then the combination with a second agent is required, especially if H₁-blockers are only partially effective.

In recent years, some reports have claimed a beneficial effect for leukotriene receptor antagonists (LT-RAs), such as montelukast and zafirlukast, as well as the 5-lipoxygenase inhibitor zileuton, for the treatment of patients with CU.⁹⁻²⁵ The effects of LT-RAs in patients with CIU have been evaluated mostly in a heterogeneous population of patients. The majority of the studies reported in the literature are anecdotal reports, and only a few are

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Abbreviations used

ASA: Acetylsalicylic acid

CIU: Chronic idiopathic urticaria

CU: Chronic urticaria

LT-RA: Leukotriene receptor antagonist

NSAID: Nonsteroidal anti-inflammatory drug

TSS: Total symptom score

placebo-controlled studies.^{19-21,23,24} Among these studies, 4 demonstrated a beneficial effect of LT-RAs,^{19-21,24} whereas one demonstrated that LT-RAs do not provide a significant therapeutic benefit in patients with CU.²³ Patient selection is very important to investigate the efficacy of LT-RAs in CIU. Exclusion criteria are all the forms of CU secondary to any known cause or the forms of CU reactivated by drugs or food additives.

In this study we compared the clinical efficacy of desloratadine, a new H₁-receptor antagonist, administered once daily as monotherapy or combined with a leukotriene antagonist (montelukast). Determining the efficacy of montelukast as monotherapy for the treatment of patients affected by CIU was also an objective of the present study.

METHODS**Patients**

We selected 160 adult patients (49 male and 111 female patients; age range, 18-69 years) with CIU from our outpatient clinic at the University Hospitals in Palermo and Verona. CIU was defined as the presence of urticarial lesions for more than 6 weeks' duration in patients with more than 3 episodes of urticaria a week without any secondary known causes. The presence of urticarial skin lesions was confirmed clinically. In all patients we have excluded the presence of positive skin test results to autologous serum and the appearance of urticaria after the administration of acetylsalicylic acid (ASA) or nonsteroidal anti-inflammatory drugs (NSAIDs) or after a challenge with food additives. Patients affected by physical or allergic urticaria or by urticaria-vasculitis were also excluded from the study. The other exclusion criteria of the study were the following: pregnancy, breast-feeding, important systemic or psychiatric disease, and habitual use of corticosteroids or LT-RAs for 2 months before entry into the study or use of oral corticosteroids in the month before the beginning of the study. Before the study began, approval was obtained from the ethics committees of the 2 centers involved. Written informed consent was obtained from all enrolled patients.

Study design

A randomized, double-blind, double-dummy, placebo-controlled, parallel-group study design was used. In each center patients received the following treatments: (1) 5 mg of desloratadine daily in the morning plus placebo of montelukast in the evening; (2) 5 mg of desloratadine daily in the morning plus 10 mg of montelukast in the evening; (3) placebo of desloratadine in the morning plus 10 mg of montelukast 1 day in the evening; or (4) placebo of desloratadine in the morning plus placebo of montelukast in the evening.

The pharmacist of the University Hospital of Verona prepared a specific set with the treatments to be used for the study. The investigators and patients were blinded with respect to the contents of each set. The pharmacist used commercially available tablets of

desloratadine (Aerius; Schering-Plough, Italy), montelukast (Singulair; Merck Sharp and Dohme, Italy), or placebo. All treatments were administered by a person unaware of who was participating in the study. Rescue medication included loratadine tablets (Clarytin, 10 mg; Schering-Plough, Italy). No other medication for urticaria was permitted during the trial.

The treatment period started after the clinical diagnosis of CIU (see below), without any run-in period. Patients were treated for 6 weeks.

Each patient attended the clinic on 4 different occasions after the diagnostic procedure. These included an initial clinic visit (visit 1), a second visit after 3 weeks of treatment (visit 2), a final visit after 6 weeks of treatment (visit 3), and a visit 2 weeks after the end of the treatment period (follow-up, visit 4).

At visit 1, symptom scores of urticaria were assessed by patients by means of a visual analog scale (0-9). Enrolled patients received a daily record diary for cutaneous symptoms. The study was conducted during 2002. All groups for each treatment included 40 patients: 20 patients (for each treatment) enrolled in Palermo and 20 patients (for each treatment) enrolled in Verona.

Before the beginning of the treatment period, a clinical history was recorded for each patient, and physical examinations and standard and specific laboratory investigations for urticaria were also performed. In particular, the following tests were performed: skin prick test for common aeroallergens and food allergens²⁶; hematologic parameter assessment (hemoglobin, red blood cell, platelet, and white blood cell counts); biochemical assessment (serum electrolytes [sodium and potassium]); indices of renal function (creatinine, urea, and urine analysis) and hepatic function (alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, and γ -glutamyl-transpeptidase); glucose-fasting testing; and C-reactive protein, serum total IgE, and antinuclear and antithyroid antibody measurement. Finally, in all patients we performed an intradermal test with autologous serum² and double-blind placebo-controlled challenges with ASA, NSAIDs, and food additives, as previously described.^{19,26,27}

Efficacy assessments

Throughout the study, disease activity was assessed by the patients with a scoring system for CIU on the basis of specific signs and symptoms.²⁸ Patients recorded the scores on their diary cards. Instruction on how to perform the assessment was provided at the time of screening. CIU signs and symptom scores were evaluated by using 4-point scales (0-3) for pruritus, number of hives, size of largest hive, interference with sleep, and interference with daily activities (Table 1).²⁸ Twice daily (morning and evening) patients scored pruritus, number of hives, and size of largest hive over the preceding 12 hours (reflective) and immediately at the time of assessment (instantaneous). These assessments were performed on awakening (before dosing) and 12 hours later. Reflective assessments of interference with sleep and daily activities were scored in the morning and in the evening only, respectively.

Safety assessments

Vital signs were recorded at all visits, whereas electrocardiography and laboratory tests were performed at screening and visit 3. All adverse events were recorded and graded for severity and potential relation to the medications used in the study.

Safety evaluations included the incidence of treatment-induced or emergency adverse events, discontinuations because of adverse events, and changes from baseline in vital signs, laboratory parameters, and electrocardiographic intervals.

Statistical analysis

The primary assessment of efficacy was based on the differences between each treatment group versus placebo for total symptom score

TABLE I. Individual signs and symptom score system²⁸

Score	Pruritus	No. of hives	Size of largest hive (cm)	Interference with sleep	Interference with daily activities
0	None	None	None	None	None
1	Mild, minimal awareness, easily tolerated	1-6	<1.25	Mild, not troublesome, adequate sleep	Mild, not troublesome, little effect on activity
2	Moderate, definite awareness, bothersome but tolerable	7-12	1.25-2.5	Moderate, awoke occasionally, average sleep	Moderate, some interference with activity
3	Severe, difficult to tolerate	>12	>2.5	Severe, substantial interference with sleep, poor sleep	Severe, daily activities substantially or completely curtailed

TABLE II. Characteristics of patients

	Desloratadine	Montelukast	Desloratadine plus montelukast	Placebo	P value
No.	40	40	40	40	
Age (y), mean (minimum and maximum)	44.0 (18-63)	44.4 (18-64)	43.7 (20-69)	43.6 (20-65)	NS
Sex (M/F)	13/27	12/28	13/27	11/29	NS
Onset of urticaria (mo)	16.6 (6-43)	16.3 (7-34)	16.9 (10-42)	17.0 (7-44)	NS
Symptoms, mean (minimum and maximum)	6.4 (5-9)	6.9 (4-9)	6.3 (5-9)	7.1 (4-9)	NS

NS, Not significant.

(TSS) and for every symptom of the urticaria. The secondary assessment was based on the differences between the group treated with desloratadine and the group treated with desloratadine plus montelukast. Data are presented as means and 95% CIs of the means of individual score. Adjusted values were subsequently averaged by patient over the entire observation period. Averages by patient were examined by using a mixed-effects ANOVA model, with the treatments (as fixed effect) and the centers (as random effect) as the main values. F values were calculated by using the mean squares of the interaction “centers × treatments” as the error term. Differences between means were performed by using the Bonferroni multiple range test (set at 95% CI). Power analysis on post hoc comparisons was performed with the GPower software package.²⁹ Comparisons are only denoted as being significant ($P < .05$, 2 tail) or not significant if our sample size exceeded the minimum sample size resulting from a power analysis at a β value of .80

RESULTS

One hundred sixty patients were randomized to treatments, with 40 patients for each treatment (see above). The baseline characteristics with respect to duration of urticaria and age of patients are reported in Table II. Only the group treated with desloratadine as monotherapy or combined therapy concluded the whole study. Twenty-seven of forty patients in the montelukast group and 35 of 40 patients in the placebo group discontinued the treatment.

Assessment of efficacy

Fig 1 and Table III show TSS, pruritus, number of hives, and size of largest hive in reflective and instantaneous evaluations. Fig 2 and Table IV show interference with daily activities and interference with sleep, respectively. Data are reported as means and 95% CIs of the means of individual scores during the treatment period and as

the mean difference (95 %CI for difference) between the treatments.

Reflective evaluation. All groups showed significant differences compared with placebo in terms of TSS, number of hives, and size of largest hive. In addition to the pruritus, only the groups treated with desloratadine as monotherapy or combined therapy showed significant differences compared with those receiving placebo, but there were no differences between the groups treated with montelukast and placebo.

Comparing the group treated with desloratadine alone and the group treated with montelukast alone, we found significant differences for TSS, pruritus, number of hives, and size of largest hive ($P < .001$, $P < .001$, $P = .017$, and $P = .003$, respectively). The comparisons between the groups treated with desloratadine plus montelukast and the group treated with montelukast alone showed significant difference for TSS, pruritus, number of hives, and size of largest hive ($P < .001$, $P < .001$, $P = .01$, and $P = .003$, respectively).

No differences were found between the group treated with desloratadine alone and the group treated with desloratadine plus montelukast.

Instantaneous evaluation. The results of the analysis of the instantaneous evaluation regarding TSS, pruritus, number of hives, and size of largest hive are similar to the results of reflective evaluation. Examining the group treated with montelukast alone versus the group treated with placebo, we found no difference for pruritus and size of largest hive, whereas there were significant differences for TSS ($P = .005$) and number of hives ($P = .001$).

In the group treated with desloratadine alone, we found significant differences for TSS ($P < .001$), pruritus ($P = .003$), number of hives ($P = .002$), and size of largest

TABLE III. Values for desloratadine, montelukast, desloratadine plus montelukast, and placebo and mean differences between the treatments for TSS (out of 9) pruritus (out of 3), number of hives (out of 3), size of hives (out of 3)

Treatments	TSS	Pruritus	Number of hives	Size of hives
Subjective symptoms of urticaria (reflective evaluation), mean (95% CI)				
DSL	1.49 (1.44-1.53)	0.50 (0.48-0.51)	0.40 (0.38-0.43)	0.41 (0.39-0.44)
MSK	2.65 (2.54-2.76)	1.20 (1.17-1.23)	0.62 (0.57-0.67)	0.66 (0.61-0.71)
DSL plus MSK	1.50 (1.44-1.57)	0.51 (0.49-0.53)	0.40 (0.38-0.44)	0.42 (0.40-0.44)
PLA	3.26 (3.17-3.36)	1.19 (1.15-1.22)	1.02 (0.97-1.07)	0.88 (0.84-0.93)
Comparisons: mean differences between the treatments (95% CI for difference); reflective evaluation				
DSL vs PLA	-1.77 (-1.89 to -1.66), <i>P</i> < .001	-0.68 (-0.72 to -0.65), <i>P</i> < .001	-0.61 (-0.67 to -0.56), <i>P</i> = .001	-0.46 (-0.52 to -0.41), <i>P</i> = .001
MSK vs PLA	-0.61 (-0.72 to -0.49), <i>P</i> < .001	0.01 (-0.02 to 0.05), <i>P</i> = NS	-0.40 (-0.45 to -0.34), <i>P</i> = .001	-0.22 (-0.28 to -0.17), <i>P</i> = .003
DSL plus MSK vs PLA	-1.76 (-1.87 to 1.64), <i>P</i> < .001	-0.67 (-0.71 to -0.63), <i>P</i> < .001	-0.61 (-0.67 to -0.56), <i>P</i> = .001	-0.46 (-0.51 to -0.42), <i>P</i> < .001
DSL vs MSK	-1.66 (-1.28 to -1.05), <i>P</i> < .001	-0.70 (-0.74 to -0.66), <i>P</i> < .001	-0.21 (-0.27 to -0.16), <i>P</i> = .017	-0.24 (-0.29 to -0.19), <i>P</i> = .003
MSK vs DSL plus MSK	1.14 (1.03 to 1.26), <i>P</i> < .001	0.69 (0.65 to 0.63), <i>P</i> < .001	0.22 (0.16 to 0.30), <i>P</i> = .01	0.24 (0.18 to 0.29), <i>P</i> = .003
DSL vs DSL plus MSK	-0.01 (-0.13 to 0.09), <i>P</i> = NS	-0.01 (-0.05 to -0.02), <i>P</i> = NS	-0.0007 (-0.05 to 0.05), <i>P</i> = NS	-0.0001 (-0.05 to 0.05), <i>P</i> = NS
Subjective symptoms of urticaria (instantaneous evaluation), mean (95% CI)				
DSL	1.81 (1.77-1.85)	0.45 (0.43-0.48)	0.54 (0.52-0.56)	0.67 (0.65-0.70)
MSK	2.86 (2.78-2.94)	1.02 (0.99-1.06)	0.77 (0.73-0.81)	0.93 (0.90-0.96)
DSL plus MSK	1.75 (1.70-1.80)	0.52 (0.50-0.55)	0.50 (0.47-0.53)	0.63 (0.61-0.66)
PLA	3.41 (3.32-3.49)	1.17 (1.11-1.23)	1.14 (1.11-1.84)	0.95 (0.90-1.01)
Comparisons: mean differences between the treatments (95% CI for difference); instantaneous evaluation				
DSL vs PLA	-1.59 (-1.68 to -1.50), <i>P</i> < .001	-0.71 (-0.76 to -0.66), <i>P</i> = .002	-0.60 (-0.64 to -0.56), <i>P</i> < .001	-0.27 (-0.32 to -0.22), <i>P</i> = .008
MSK vs PLA	-0.54 (-0.63 to -0.45), <i>P</i> = .005	-0.14 (-0.19 to 0.01), <i>P</i> = NS	-0.37 (-0.41 to -0.32), <i>P</i> = .001	-0.02 (-0.07 to 0.02), <i>P</i> = NS
DSL plus MSK vs PLA	-1.65 (-1.74 to 1.56), <i>P</i> < .001	-0.64 (-0.69 to -0.59), <i>P</i> = .002	-0.64 (-0.68 to -0.60), <i>P</i> < .001	-0.32 (-0.36 to -0.27), <i>P</i> < .001
DSL vs MSK	-1.04 (-1.14 to -0.95), <i>P</i> = .001	-0.57 (-0.62 to -0.51), <i>P</i> = .003	-0.23 (-0.27 to -0.18), <i>P</i> = .002	-0.25 (-0.29 to -0.20), <i>P</i> = .008
MSK vs DSL plus MSK	1.10 (1.01 to 1.20), <i>P</i> = .001	0.50 (0.45 to 0.55), <i>P</i> = .004	0.27 (0.22 to 0.31), <i>P</i> = .001	0.29 (0.24 to 0.34), <i>P</i> = .007
DSL vs DSL plus MSK	0.05 (-0.03 to 0.15), <i>P</i> = NS	-0.006 (-0.11 to 0.01), <i>P</i> = NS	0.004 (-0.03 to 0.08), <i>P</i> = NS	0.04 (-0.004 to 0.09), <i>P</i> = NS

DSL, Desloratadine; MSK, montelukast; PLA, placebo; NS, not significant.

TABLE IV. Mean values for desloratadine, montelukast, desloratadine plus montelukast, and placebo and mean differences between the treatments for interference with sleep (out of 3) and interference with daily activities (out of 3)

Treatments	Interference with sleep (95% CI)	Interference with daily activities (95% CI)
DSL	0.60 (0.58-0.62)	0.35 (0.33-0.37)
MSK	1.00 (0.97-1.03)	0.41 (0.37-0.44)
DSL plus MSK	9.72 (0.69-0.75)	0.40 (0.38-0.42)
PLA	1.03 (0.99-1.07)	0.87 (0.84-0.90)
Comparisons: mean differences between the treatments (95% CI for difference)		
DSL vs PLA	-0.43 (-0.47 to -0.39), <i>P</i> = .003	-0.52 (-0.55 to -0.48), <i>P</i> = .001
MSK vs PLA	-0.03 (-0.07 to 0.01), <i>P</i> = NS	-0.46 (-0.50 to -0.43), <i>P</i> = .002
DSL plus MSK vs PLA	-0.31 (-0.35 to -0.27), <i>P</i> = .007	-0.47 (-0.50 to -0.44), <i>P</i> = .002
DSL vs MSK	-0.40 (-0.44 to -0.35), <i>P</i> = .003	-0.06 (-0.09 to -0.02), <i>P</i> = NS
MSK vs DSL plus MSK	0.28 (0.24 to 0.32), <i>P</i> = .01	0.0002 (-0.03 to 0.03), <i>P</i> = NS
DSL vs DSL plus MSK	-0.11 (-0.16 to -0.07), <i>P</i> = NS	-0.05 (-0.08 to -0.01), <i>P</i> = NS

DSL, Desloratadine; MSK, montelukast; PLA, placebo; NS, Not significant.

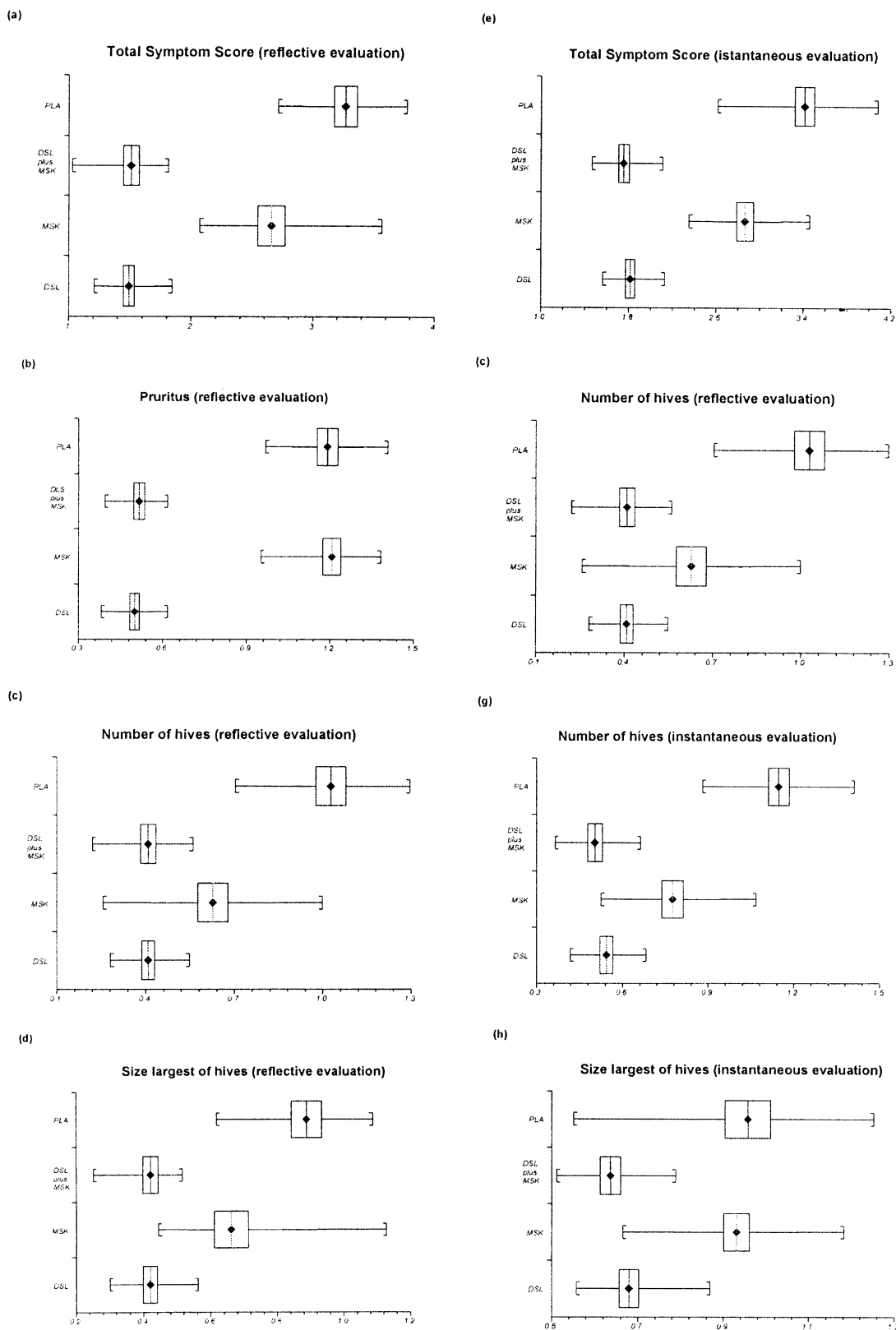


FIG 1. Subjective symptoms of urticaria, TSS, pruritus, numbers of hives, and size of largest hive as reflective and instantaneous evaluations. Data are reported as means with 95% CIs of the mean of individual scores during the treatment period. The comparison between treatments is reported in [Table III](#).

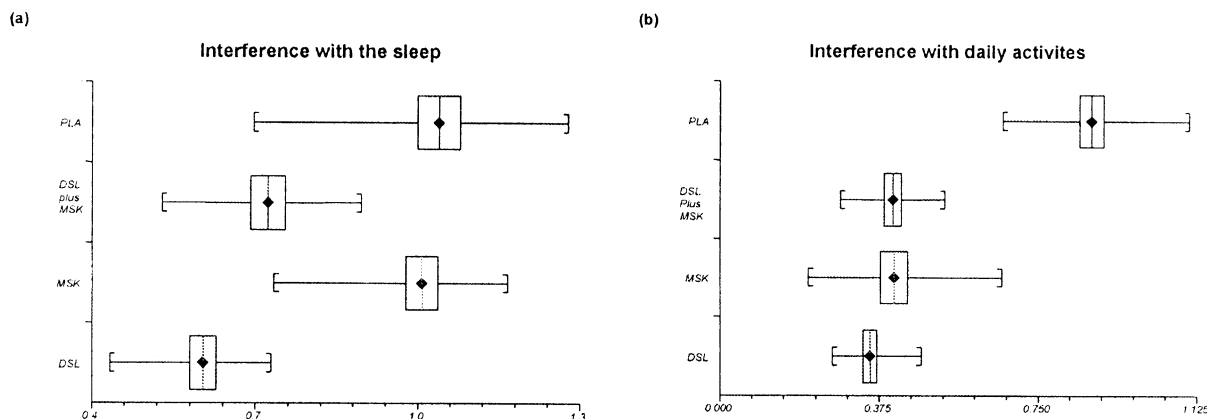


FIG 2. Interference with sleep and interference with daily activities. Data are reported as means with 95% CIs of the mean of the individual scores during the treatment period. The comparison between treatments is reported in Table IV.

hive ($P = .008$) in comparison with the group treated with montelukast alone. We obtained similar results comparing the group treated with desloratadine plus montelukast and the group treated with montelukast alone for TSS ($P = .001$), pruritus ($P = .004$), number of hives ($P = .001$), and size of largest hive ($P = .007$). We found no significant differences between the group treated with desloratadine alone and the group treated with desloratadine plus montelukast.

Interference with sleep. Regarding interference with sleep, significant differences were found between the groups treated with desloratadine, both as monotherapy and as combined therapy with montelukast, in comparison with the placebo group ($P = .003$ and $P = .007$, respectively). Comparing the group treated with desloratadine alone versus the group treated with montelukast alone, we found significant differences ($P = .003$). Also, significant differences were found comparing those treated with montelukast alone versus those treated with desloratadine plus montelukast ($P = .01$). In addition, no differences were found between the group treated with montelukast alone versus the group treated with placebo and between the group treated with desloratadine alone versus the group treated with desloratadine plus montelukast.

Interference with daily activities. Considering daily activities, we found significant differences between all active treatments and the placebo group. We found no differences among the groups treated with desloratadine alone, montelukast alone, and desloratadine plus montelukast.

Use of rescue medication. The use of rescue medication, expressed as the median number of days without the use of loratadine tablets, was significantly lower in the groups treated with desloratadine as monotherapy (90.6 days) or combined therapy (91.0 days) than in the montelukast-treated group (45.2 days, $P < .001$) or the placebo-treated group (54.0 days, $P < .001$). We found no differences between the group treated with desloratadine and the group treated with desloratadine plus montelukast

and between the group treated with montelukast and the group treated with placebo.

Safety

A low incidence of adverse events was observed in the study. All adverse events were rated as mild. Exacerbation of urticarial symptoms was reported in 27 patients in the group treated with montelukast and in 35 patients in the group treated with placebo.

DISCUSSION

The results of this study demonstrate that desloratadine administered once daily is more effective than montelukast for the treatment of urticarial symptoms in patients with moderate CIU. The combination of desloratadine with montelukast failed to produce a substantial advantage for urticarial symptoms in comparison with desloratadine administered in monotherapy. Moreover, treatment with montelukast as monotherapy failed to control the urticarial symptoms, such as pruritus, in our study in patients affected by CIU.

In this study we evaluated only patients affected by moderate CIU. We excluded patients with positive challenge results to ASA, NSAIDs, or food additive; those with positive cutaneous test results to autologous serum; or both. We also excluded patients who reported an aggravation of their symptoms through pressure. Therefore the absence of these triggers indicates the presence of an idiopathic form of urticaria. Angioedema was rarely present in this group of patients. This is an important difference compared with some of the previous reports, in which patients were selected without precise characteristics.^{20,21,23}

In patients with moderate CIU, the role of leukotrienes is probably rather insignificant.²⁴ In a previous study we examined patients with CIU and with CU who had ASA or food additive sensitivity, determining urinary metabolite concentrations of both histamine and leukotrienes.³⁰ The 2

groups of patients affected by CU had markedly increased urinary concentrations of methylhistamine at baseline, thus allowing a clear distinction from the control group (healthy volunteers). On the contrary, when we compared urinary leukotriene E₄ levels in the same subjects, we found no difference at baseline in the 3 groups but an increase in leukotriene levels after challenge only in patients with ASA or food additive sensitivity. These results might also explain the low clinical response to therapy with LT-RAs in patients with CIU with no well-defined triggers. Recently, the results of the study by Bagenstose et al²⁴ would confirm that the treatment of combined therapy with H₁-receptor antagonists and LT-RAs is effective only in patients with autoimmune and more severe urticaria (positive skin test response to autologous serum).^{24,31}

Finally, we should consider the economic aspect of the treatments: the cost of an anti-H₁-receptor treatment is 0.53€ per day, whereas the daily cost of an antileukotriene receptor treatment is 2.02€ per day. Particularly, the consumption of rescue medication (loratadine) is similar in patients treated with montelukast as monotherapy and in patients treated with placebo, and these data confirm that histamine is the most important mediator of the CIU.

In conclusion, the results of this comparative study demonstrate that desloratadine, regularly administered once daily, is effective for the treatment of urticarial symptoms, confirming the results of other studies.^{28,32}

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