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Desloratadine in combination with montelukast in the treatment of chronic urticaria: a randomized, double-blind, placebo-controlled study

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Summary

Background Chronic urticaria (CU) is a common skin condition. It is frequently a disabling disease due to the persistency of clinical symptoms, the unpredictable course and negative influence on the quality of life.

Objective The aim of this study is to determine whether montelukast, a LTD4 receptor antagonist, plus desloratadine, is more efficacious than desloratadine alone in the treatment of chronic urticaria.

Materials A randomized, double-blind, placebo-controlled study was conducted on 81 patients with a diagnosis of CU. A 1-week single-blind placebo run-in period (baseline) was followed by a 6-weeks double blind active treatment period. The patients were randomized to receive the following treatment once daily: (a) oral desloratadine (5 mg) plus placebo; (b) desloratadine (5 mg) plus montelukast (10 mg); (c) oral placebo alone. The study ended after another 1-week single-blind placebo washout period.

Results The evaluable population thus consisted of 76 patients. Both desloratadine alone and desloratadine plus montelukast administered once daily yielded improvements with respect to the baseline assessment as regards pruritus, number of separate episodes, size and number of weals, visual analogue score and patients' quality of life and with respect to the placebo group both in the active treatment period and in the run-out period. However, desloratadine plus montelukast was shown to improve the symptoms and patients' quality of life significantly more than desloratadine alone, although it did not have a significant effect on the number of urticarial episodes.

Conclusion The combination of desloratadine plus montelukast is effective in the treatment of CU. It may therefore be a valid alternative in patients with relatively mild CU, in view of its efficacy and the lack of adverse events.

Keywords chronic urticaria, desloratadine, montelukast, placebo-controlled

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Introduction

Chronic urticaria (CU) is classically defined as the occurrence of weals on most days for more than six weeks; when there are no causal agents, it is defined as idiopathic (CIU). It is a common skin condition that affects 0.1–3% of people in the USA and Europe and accounts for nearly 75% of all CU cases [1, 2]. The course and duration of CU are highly variable and unpredictable. Spontaneous remission may often occur within 12 months, but a substantial number of patients may have symptoms lasting periodically for years or suffer irritating symptoms such as pruritus for decades [3, 4]. CU is frequently a disabling disease due to the persistency of clinical symptoms, the unpredictable course and negative influence on the quality of life, as it can cause sleep disruption, fatigue, social isolation, energy loss and emotional/sexual disturbances [5]. From a questionnaire administered to urticaria patients, O'Donnell et al. [5] established that the disability described by patients is comparable to that of patients with ischemic heart disease. Successively, Finlay et al. [6] developed the Dermatology Life Quality Index (DLQI). They used it to measure and compare the disability induced by a variety of common dermatological conditions and suggest that the questionnaire can be administered before and after treatment interventions, to serve as an indicator of treatment efficacy.

The goal of treatment in CU is to ensure rapid and prolonged control of the symptoms and a rapid return to normal social activities. Non-sedating H1-receptor antagonists are the primary treatment. In particular, desloratadine is a new, selective, histamine H1-receptor antagonist and also inhibits the generation of many other inflammatory mediators by mast cells, basophils and other cells involved in the allergy cascade. It is the biologically active metabolite of the second generation antihistamine, loratadine, and exhibits both anti-allergic and anti-inflammatory effects (*in vitro*, desloratadine has been proven to inhibit cysteinyl-leukotrienes (Cys-LTs) release) [7]. In CIU patients, desloratadine

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provides rapid and enduring relief of pruritus, reduces the number and size of hives, relieves sleep disturbances and improves daily living activities [8]. Nevertheless, CU is often difficult to treat and may not be controlled by antihistamines alone. It has been postulated that mediators other than histamine such as kinins, prostaglandins and leukotrienes (LTs), may be responsible for some of the symptoms in urticaria that cannot be controlled by antihistamines [9]. In particular, LTs are unsaturated fatty acids generated by actions of the 5-lipoxygenase enzyme on the cell membrane-bound arachidonic acid. Once secreted extracellularly, LTs act on specific receptors and are then rapidly degraded. LTs, released from dermal mast cells, are an important contributory factor to the clinical manifestations of urticaria. They increase the permeability of capillaries and small veins, which results in weal formation. The itching and pain are caused by the consequent sensory nerve stimulation. In fact, intradermal injection of LTs has been shown to induce a weal-flare reaction, providing further evidence that these mediators may participate in the formation of urticaria [10]. Some reports have claimed a beneficial effect of the LT receptor antagonists, zafirlukast and montelukast, as well as of the 5-lipoxygenase-inhibitor zileuton, in the treatment of patients with CU, although these results have not been confirmed [11–14]. The aim of this study is to determine whether montelukast, a LTD4 receptor antagonist, plus desloratadine, is more efficacious than desloratadine alone in the treatment of CU.

Methods

A randomized, double-blind, placebo-controlled study was conducted on 81 patients with a diagnosis of chronic urticaria (58 women and 23 men) ranging in age from 15 to 71 years (mean 37.5 ± SD 12.3 years).

All patients completed screening prior to treatment; exclusion criteria were physical urticaria, or urticaria caused by medications, insect bites, food or other known causes, as well as a history of atopic diseases. Drug-induced urticaria was excluded only by the patient history.

After taking a careful history, where appropriate, a challenge test was performed to exclude a delayed pressure urticaria: a 7 kg weight was suspended from the patient's shoulder for 15 min and reading of the test area was done at 30 min, 3, 6, 8 and 24 h [15].

Patients with significant concomitant illness (e.g. malignancies or psychiatric, hepatic, endocrine or other major systemic diseases) were also excluded. Sufficient washout time was required for previous urticaria treatments (especially long-acting antihistamines and corticosteroids) before the study drugs were administered.

Approval for the study was obtained from the Ethics Committee and all patients gave their written informed consent.

Study design

Patients were administered placebo, desloratadine plus placebo or desloratidine plus montelukast, and were not informed that the treatment would be divided up into specific periods.

A 1-week single-blind placebo run-in period (baseline), was followed by a 6-weeks double-blind active treatment period. The 81 patients were randomized to receive the following treatment once daily : (a) oral desloratadine (5 mg) plus placebo; (b) desloratadine (5 mg) plus montelukast (10 mg); (c) oral placebo alone. The study ended after another 1-week single-blind placebo washout period.

Each patient was examined by the physician four times over the 8-week period: this included (apart from the initial screening visits), a 1st visit following the placebo run-in; a 2nd visit after 3 weeks of active treatment; a 3rd visit after 6 weeks of active treatment (end of treatment), and a final visit at the end of the second placebo washout period (follow-up).

The tablets were encapsulated in a double-blind fashion, and sealed in envelopes by a pharmacist along with the instructions sheets at the beginning of the trial. All treatments were dispensed by a third party.

Medications that could interfere with the clinical evaluations and systemic or topical medication for urticaria, other than those specified in the study treatment, were not allowed during the trial.

Efficacy measures

Throughout the study, all patients recorded their symptoms in a daily diary, including pruritus, size of weals, number of weals, number of separate urticarial episodes. At each clinical visit the patient's diary was reviewed, the patient was interviewed as to the event/s occurring in the previous week/s, and a physical examination was performed. Evaluations were made at each visit by the same investigator for each patient.

Efficacy measures were scored according to the following scales: Pruritus: 0 (none), 1 (mild), 2 (moderate) and 3 (severe); Number of weals: 0 (none), 1 (1–10 weals), 2 (11–20 weals), 3 (>20 weals); Average size of weals: 0 (no lesion), 1 (<1.27 cm), 2 (1.27–2.54 cm), 3 (>2.54 cm); Number of separate urticarial episodes: 0 (no episodes), 1 (1 episode), 2 (2–3 episodes), 3 (>3 episodes).

The maximum value of the total symptom score (TSS) was 12.

At each clinical visit, patients also completed a 10 cm visual analogue score (VAS) indicating the overall severity of their urticaria over the previous days from 0 (none) to 10 (worst).

Urticaria quality of life (QOL)

A five-question urticaria QOL questionnaire was administered at each clinical visit, evaluating the following domains: cutaneous symptoms, emotions, practical problems. The questions were: 'Over the last week, how itchy, sore, painful or stinging has your skin been?'; 'Over the last week, how embarrassed or self-conscious have you been because of your skin?'; 'Over the last week, how much has your skin influenced the clothes you wear?'; 'Over the last week, how much has your skin affected any social or leisure activities?'; and 'Over the last week, has your skin prevented you from working or studying? If 'No', over the last week how much has your skin been a problem at work or studying?'. These are part of the DLQI [6].

Patients scored their response to each question on a four-point scale ranging from 0 (no problems) to 3 (severe problems).

Safety

Safety and tolerability were assessed on the basis of the adverse events referred or changes in vital signs, physical examination findings, and electrocardiograms recorded before and at the end of treatment. Laboratory safety parameters (haematology, serum biochemistry and urine analysis) were assessed before and after the treatment period.

Statistical analysis

The significance of differences in age, sex, baseline symptoms severity score and baseline QOL score, baseline duration of urticaria score, baseline VAS was compared using the Kruskal–Wallis test for continuous data and the χ^2-test for categorical data.

For the efficacy analyses and comparison of the VAS in each study group, and at different visits the Wilcoxon signed-rank test was used. To compare the efficacy and the VAS in the three groups at different visits the Mann–Whitney test was performed.

In all instances, a probability value <0.05 was considered statistically significant.

Results

The 81 patients were randomized, 27 were treated with desloratadine plus montelukast (23 women and 4 men) ranging in age from 15 to 67 years (mean 35.6 ± SD 12.8 years); 27 were treated with desloratadine alone (20 women and 7 men) ranging in age from 18 to 71 years (mean 37.5 ± SD 10.9 years); 27 were treated with placebo alone (15 women and 12 men) ranging in age from 20 to 66 years (mean 38.4 ± SD 11.7 years). The three groups were balanced with respect to baseline demographic data, including patient age and sex, duration of disease, overall symptom severity and perceived QOL. One patient in the desloratadine plus montelukast group, two patients in the desloratadine group and two in the placebo group discontinued treatment during the first study week. The reasons for discontinuation were: non-compliance ($n = 3$); lack of desire to continue ($n = 1$) and the need to take oral corticosteroids because of an episode of acute angioedema ($n = 1$).

The evaluable population thus consisted of 76 patients. The patient demographics and baseline characteristics are given in Table 1.

Table 1. Baseline patients data (only patients who completed the study)

Patients data	Desloratadine	Desloratadine + montelukast	Placebo
Sex			
Male	6 (24%)	4 (15.4%)	10 (40%)
Female	19 (76%)	22 (84.6%)	15 (60%)
Age (years)			
Mean ± SD	37.5 ± 10.9	35.6 ± 12.8	36.8 ± 10.7
Symptoms severity (overall score)*	59.7 ± 13.4	63 ± 10.8	60.7 ± 9.4
QOL (overall score)†	32.8 ± 6.9	32.8 ± 9.1	31.4 ± 6.1
Duration of urticaria (months)	8.24 ± 5.5	12.3 ± 24.1	8.9 ± 4.1
Baseline VAS	8.8 ± 1.33	9.3 ± 1.2	8.6 ± 1.03

QOL, Quality of life; VAS, Visual analogue score.
*Mean of 4 domains scored on 0–3 scale. †Mean of the 5 domains scored on 0–3 scale.

Efficacy analysis

At all study visits, patients from the treatments groups (desloratadine plus montelukast group and desloratadine alone group) reported a significant improvement in overall CU conditions compared with placebo group, and this effect was maintained in the follow-up analysis ($P<0.05$).

At all study visits, patients treated with desloratadine plus montelukast reported a significant improvement in overall urticaria conditions compared with desloratadine alone, and this effect was maintained in the follow-up analysis. The mean TSS value decreased by 88.5% at the end of therapy with respect to the baseline evaluation in the group treated with desloratadine plus montelukast, and by 69% in the group treated with desloratadine only (Fig. 1). At the end of the active treatment, total disappearance of the symptoms was recorded in 4 (16%) vs. 19 (73%) patients treated with desloratadine or desloratadine plus montelukast, respectively. Controls conducted one week after the interruption of active treatment showed that the positive effects persisted and are still statistically significant between the two groups, although to a lesser degree compared to those obtained during active therapy (Table 2). At follow-up, total disappearance of the symptoms was recorded in 2 (8%) vs. 5 (19.2%) patients previously treated with desloratadine or desloratadine plus montelukast, respectively.

Pruritus

Results in the treatments groups were significantly better than in the placebo group in reducing the pruritus score throughout the trial ($P<0.05$).

Desloratadine plus montelukast was statistically superior to desloratadine alone in reducing mean pruritus scores throughout the active treatment (Table 2). In the desloratadine plus montelukast group, this combination determined a reduction in pruritus intensity at all visits except follow-up, when the pruritus score was higher than those reported at

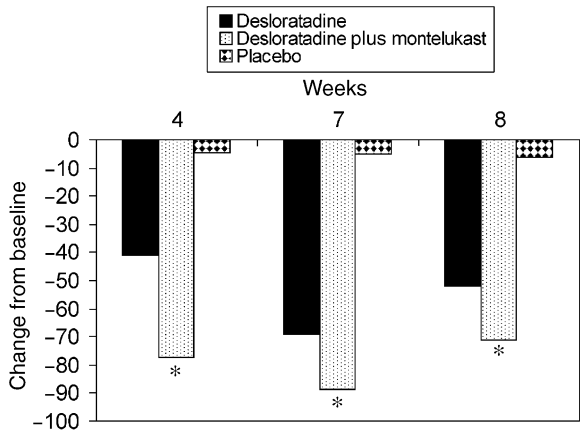

Fig. 1. Overall symptoms scores compared to baseline. *$P<0.05$ for desloratadine plus montelukast vs. desloratadine alone; all *P*-values for the treatment groups vs. placebo were <0.05.

Table 2. Urticaria symptoms scores with desloratadine or desloratadine plus montelukast

	Change from baseline (mean differences)											
	Week 4				Week 7				Week 8			
	P	D	D+M	*P*-value*	P	D	D+M	*P*-value*	P	D	D+M	*P*-value*
Overall score (mean of 4 domains)	−0.5	−3.9	−7.5	<0.05 ($T=855$)	−0.4	−6.6	−8.2	<0.05 ($T=794$)	−0.6	−5	−7	<0.05 ($T=830.5$)
Number of weals	−0.2	−1.2	−2.1	<0.05 ($T=3.5$)	−0.3	−1.8	−2.4	<0.05 ($T=3.6$)	−0.2	−1.5	−1.8	<0.05 ($T=2.1$)
Number of separate urticarial episodes	−0.1	−0.9	−1.5	>0.05† ($T=1.8$)	−0.04	−1.4	−1.6	>0.05† ($T=0.3$)	−0.08	−1.2	−1.7	>0.05† ($T=1.9$)
Size of weals	−0.04	−0.7	−1.8	<0.05 ($T=3.4$)	−0.04	−1.7	−2.3	<0.05 ($T=3.5$)	−0.2	−0.9	−1.5	<0.05 ($T=3.1$)
Pruritus	−0.04	−1.1	−2	<0.05 ($T=4.1$)	−0.2	−1.8	−2.2	<0.05 ($T=2.7$)	−0.1	−1.5	−1.8	>0.05† ($T=1.6$)

P, placebo; D, desloratadine; D+M, desloratadine+montelukast.
All *P*-values for the treatment groups vs. placebo were <0.05.
**P*-value for desloratadine plus montelukast vs. desloratadine. †Not significant.

week 7 (Fig. 2). Instead, in the desloratadine group, there was a constant significant improvement of the pruritus score, throughout the active treatment, while at follow-up the symptoms had worsened with respect to the active period ($W=-49$; $P>0.05$). At the end of the active treatment, a reduction in pruritus severity was recorded compared with baseline by 69.9% in the desloratadine group and by 80.3% in the desloratadine plus montelukast group ($P<0.05$). At follow-up, the reduction in pruritus severity compared with baseline was 58.7% in the desloratadine group and 71.3% in the desloratadine and montelukast group ($T=1.6$; $P>0.05$).

In the placebo group there were only slight but not significant changes of the pruritus score during the entire trial (Fig. 2).

Number of weals

The treatments groups were statistically superior to the placebo group in terms of reduction of the number of weals score throughout the trial ($P<0.05$).

During the first three active treatment weeks desloratadine plus montelukast therapy produced a 79.9% reduction in the number of weals scores compared with baseline, as against a 46.3% reduction in the desloratadine group. This effect was maintained up to the end of the trial and at follow-up: at week 7 there was a 90% reduction with montelukast plus desloratadine and a 65.7% reduction with desloratadine only. At follow-up, the reduction in the group treated with montelukast plus desloratadine was 71.8% vs. 55.2% in the group treated with desloratadine alone ($P<0.05$).

Thus, desloratadine plus montelukast treatment produced a significant reduction in the number of weals score throughout the trial ($P<0.05$). Desloratadine treatment produced a significant reduction in the number of weals score throughout the active treatment period, while at follow-up there was not a significant worsening of this score with respect to the active treatment period ($W=-42$; $P>0.05$). In the placebo group there were only slight but not significant changes in the number of weals score during the entire trial (Fig. 2).

Number of separate urticarial episodes

Both the treatments groups were statistically superior to the placebo group in terms of reduction of the number of urticarial episodes scores throughout the trial ($P<0.05$).

During the first three active treatment weeks desloratadine plus montelukast therapy produced an 82.9% reduction in the number of separate episodes score compared to baseline, as against a 55% reduction in the desloratadine group ($T=1.8$; $P>0.05$). This marked effect did not persist at the end of the active treatment, whereas there was a major reduction, although not significant, in the desloratadine group (85% vs. 82.9%). At the follow-up visit, again desloratadine plus montelukast treatment was associated with a greater,

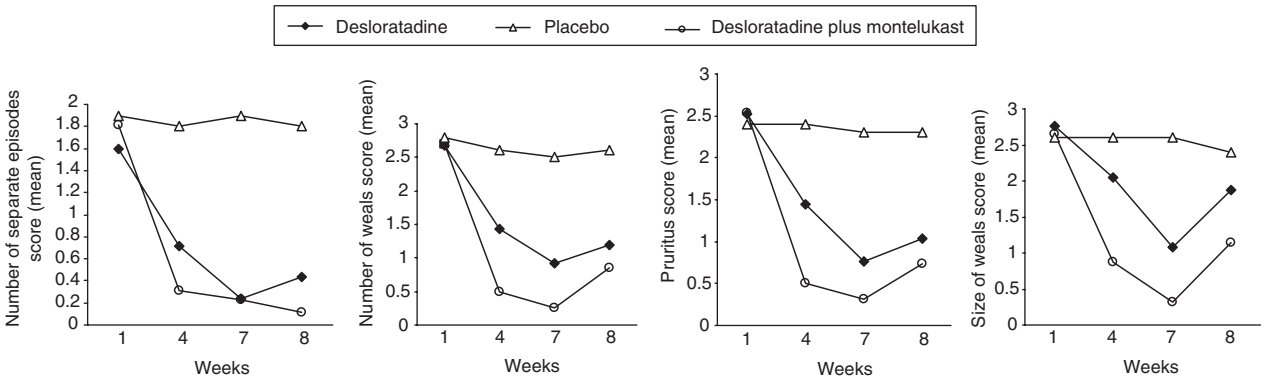

Fig. 2. Mean symptoms scores by week of treatment.

although not significant, reduction as compared to baseline (91.7% vs. 72.5%; $T = 1.9$; $P > 0.05$) (Fig. 2).

Therefore, desloratadine plus montelukast treatment produced a significant reduction in the number of urticaria episodes during the first three active treatment weeks, while at week 7 there was a reduction of the score, although this was not significant ($P > 0.05$); at follow-up there was a worsening of this score with respect to the active period ($W = -12$; $P > 0.05$).

The same trend was observed in the desloratadine group: in fact treatment with desloratadine alone produced a significant reduction in the number of episodes score throughout the first three active treatments weeks, at week 7 there was a reduction in the score, although this was not significant ($P > 0.05$) and at follow-up there was a worsening of this score with respect to the active period ($W = -25$; $P > 0.05$).

In the placebo group there were only slight, but not significant changes in the number of urticarial episodes score during the entire trial (Fig. 2).

Size of weals

Both the treatment groups were statistically superior to the placebo group in terms of reduction of the size of weals score throughout the trial ($P < 0.05$).

The results obtained for the size of weals score with desloratadine plus montelukast were again significantly better than those with desloratadine alone, after the first three weeks of active treatment (-66.8% vs. -26.1%; $P < 0.05$). The effect was maintained for the duration of the study. At the end of the active treatment, the reduction was 88.3% in the desloratadine plus montelukast group and 60.9% in the desloratadine group, compared to baseline ($P < 0.05$). At follow-up, the reduction was 64.3% in the desloratadine plus montelukast group, and 31.9% in the desloratadine group ($P < 0.05$).

Thus, desloratadine plus montelukast treatment produced a significant reduction in the size of weals score throughout the active treatment period, but at follow-up there was a significant worsening of this score ($P < 0.05$). The same observations were made in the desloratadine group, the worsening at follow-up being again significant ($P < 0.05$). In the placebo group there were only slight, but not significant changes in the size of weals score during the entire trial (Fig. 2).

QOL

There was a significant improvement in overall QOL with respect to baseline in the two treatment groups, while in the placebo group there were a little, but not significant improvement. However, the improvement in the desloratadine plus montelukast group was significantly greater than in the desloratadine group both at the end of the study and at each clinical visit during the study (Fig. 3).

VAS

As shown in Fig. 4, there was a significant improvement in the VAS with respect to baseline in the two treatment groups, while there were only slight changes among placebo-treated patients. Patients in the desloratadine plus montelukast treatment group indicated a mean decrease from baseline of

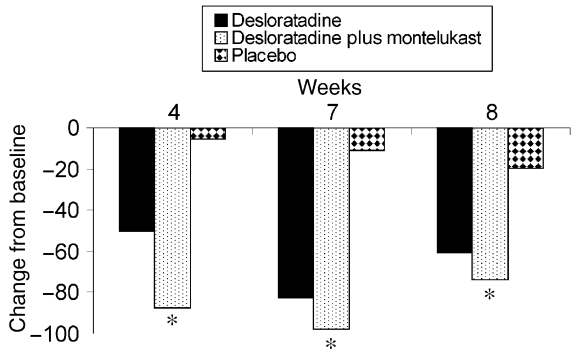

Fig. 3. Quality of life score compared to baseline. *$P < 0.05$ for desloratadine plus montelukast vs. desloratadine alone; all *P*-values for the treatment groups vs. placebo were < 0.05.

77.7% after 3 weeks of active treatment, 87.7% after 6 weeks and 73.6% at follow-up ($P < 0.05$).

The corresponding decreases in patients treated with desloratadine only were 50%, 72.5% and 61.3%, ($P < 0.05$). Thus the desloratadine plus montelukast group had a significantly greater improvement in the VAS, as indicated in all visits, than the desloratadine group.

Safety

No clinically significant changes in vital signs, laboratory parameters, or ECG criteria occurred during the study in all groups. No patient reported any side-effects during the course of therapy in all study groups.

Discussion

This is the first double-blind placebo-controlled study to demonstrate the therapeutic benefit of montelukast sodium (10 mg) given concomitantly with desloratadine (5 mg) in patients with CU. In this study, both desloratadine alone and desloratadine plus montelukast administered once daily yielded improvements with respect to the baseline assessment as regard to pruritus, number of separate urticarial episodes, size and number of weals, VAS and patients' QOL and with respect to

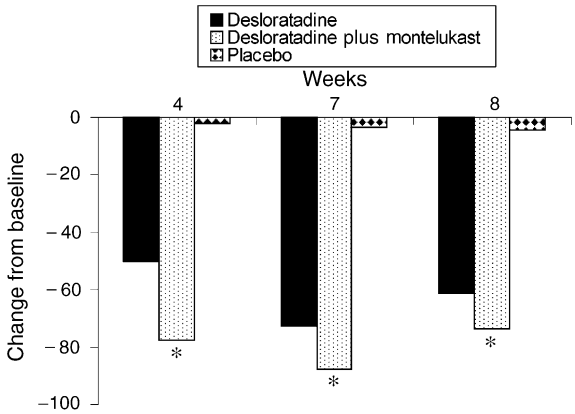

Fig. 4. Visual analogue score compared to baseline. *$P < 0.05$ for desloratadine plus montelukast vs. desloratadine alone; all *P*-values for the treatment groups vs. placebo were < 0.05.

the placebo group both in the active treatment period and in the run-out period. However, desloratadine plus montelukast was shown to improve the symptoms and patients' QOL significantly more than desloratadine alone, except for the number of separate episodes, for which although the association did yield a stronger action, this increase was not significant. This greater efficacy could be because the combination of the two drugs can interfere with more mediators of the complex hierarchy of urticaria mediators than the single drug; e.g., while desloratadine interferes with Cys-LTs production, montelukast interferes with the LTD4 receptors.

This was observed after the first three treatment weeks and persisted at one week after the end of active treatment, so the effects were maintained over time. Nevertheless, there was a worsening of the scores at follow-up with respect to the active treatments periods in both treatment groups.

In this study we did not perform any tests (autologous serum skin test (ASST) or *in vitro* basophil and mast cells histamine release assay) to demonstrate the presence of autoantibodies which degranulate mast cells and basophils by binding high affinity IgE receptors or IgE bound to them. This would lead to considering the CU as autoimmune urticaria.

This is also why we have not used the term 'idiopathic' for the afflictions described in this study, because without any evidence on the presence or absence of functional autoantibodies we cannot exclude a diagnosis of autoimmune urticaria.

The clinical features of patients with autoimmune urticaria have been well defined by Sabroe et al. [16] who found that in presence of autoantibodies, identified by *in vitro* testing, patients have a more severe disease subtype as regards urticaria weal numbers, weal distribution, itching severity, and associated systemic features than patients without autoantibodies. However, more recently, we have studied the features of patients with autoimmune CU and we noted that for most of the parameters, we examined to define the severity of urticaria (weal number, weal size and itching), no significant difference was found between patients with a positive ASST and patients with a negative test. Only the incidence of angioedema was significantly different in the two groups, but this is not sufficient to indicate that patients with a positive ASST had more severe urticaria [17].

So, although we know the limitations of the ASST and the real significance of these autoantibodies, we cannot conclude that autoimmune urticaria is a more severe clinical presentation of CU.

Various studies in literature have addressed the use of desloratadine and montelukast in the treatment of other allergic diseases, in particular asthma and rhinitis [18–20].

As regard to CU, the efficacy of montelukast alone or desloratadine alone has been evaluated. Recent, multi-centre, randomized trials have demonstrated that desloratadine exerts marked antipruritic effects and also significantly reduces the number and size of wheals. In a double-blind placebo-controlled study in CIU patients, desloratadine (5 mg) once daily conferred significant first-dose symptom relief that endured throughout the 24-h dosing interval and weekly through the treatment weeks. Marked symptom relief was accompanied by significant improvements in both sleep patterns and daily activities at these time points [8]. Anti-LTs were successfully used alone to treat several urticaria types: exercise-induced cholinergic urticaria, delayed pressure urticaria, cold urticaria, CIU and to prevent urticaria exacerbations following the use of NSAIDs in some patients with CU [21–24].

In addition, anti-LTs were effective to treat patients with unremitting, steroid-dependent urticaria and patients with CU, NSAIDs and hypersensitivity to food additives [25, 26]. Notwithstanding these encouraging results, Reimers et al. [14] found no significant difference between 20 mg zafirlukast daily and placebo for any of the efficacy measures (daily symptom score, overall assessment by patients and investigating physician).

They observed 19 cases (41.3%) of resolution of CU but considered these as spontaneous remission because, as is well known, the course of CU may be highly variable. They concluded that LTs have no significant role in the etiology of CU.

A number of studies have shown that the combination of antihistamines and anti-LTs in asthma and allergic rhinitis is more efficacious than single treatment, although the combination of desloratadine plus montelukast has not previously been evaluated [18–20]. The combination of antihistamines and anti-LTs has not been much used to treat urticaria, although in the study by Norris [27], 60% of patients had an improvement of their severe urticaria following therapy with zafirlukast and antihistamines. Recently, we have demonstrated the efficacy of the combination to treat delayed pressure urticaria [15]. In the present study the efficacy of combined therapy was also estimated by administering a questionnaire probing the QOL of life, because the clinician's view of the disease severity does not always correlate with the patient's perception of the deriving disability. The constant improvement of the QOL during the weeks of study, as reported by our patients both on the basis of the questionnaire and the VAS, highlights the greater effectiveness of treatment with desloratadine plus montelukast than desloratadine alone.

Our findings imply that H1-receptor antagonists and Cys LT1 antagonists may have complementary effects on the mechanism of CU. In our experience this drug combination was really effective in the treatment of urticaria and we do not believe the remission or improvement of the urticaria obtained was spontaneous because the excellent results were recorded right from the first 3 weeks of active treatment. This combination therapy may therefore be advantageous in view of its efficacy and the lack of adverse events, in patients with relatively mild CU without known precipitating factors.

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