ORIGINAL CONTRIBUTIONS

A MULTICENTRIC TRIAL OF LORATADINE AND CETIRIZINE IN URTICARIA

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Two hundred and ten patients with chronic urticaria were divided into two groups; one group was treated with Loratadine 10mg daily while the other with cetirizine 10mg daily. The total duration of treatment was four weeks. Pretreatment and post-treatment evaluations were made. It was noticed that loratadine was superior to cetirizine in terms of a rapid onset of actions, overall clinical efficacy and minimal side effects.

Key words : Urticaria, Loratadine, Cetirizine

Introduction

In urticaria, H1 receptors mediate the pruritic, vasodilatory and vasopermeable actions of histamine.[1-3] Apart from their specific H1 receptor inhibitory action, the first generation H1 antagonists also activate muscarinic, cholinergic, serotonergic and alpha-adrenergic receptors, leading to side effects.[4] The second generation antihistamines cetirizine and loratadine selectively antagonise H1 receptors lessening the possibility of side effects. Both drugs inhibit the release of histamine from human basophils. Loratadine, in addition, inhibits other inflammatory mediators like PGD2 and LTC_4[5-6] via interference with calcium transport across the cell membrane[7] and the expression of adhesion molecules[8] which may be either from the selectin, immunoglobulin or integrin families and are involved in the aetiopathogenesis of allergic inflammation. These drugs also offer the advantage of once daily dosing. Since there is no Indian report of a comparative trial of these drugs in chronic urticaria, we performed a randomized investigator-blinded parallel group study to compare

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their efficacy and side effects in the treatment of this common condition.

Materials and Methods

Two hundred and ten patients in the age group of 12 to 60 years suffering from urticaria for at least 6 weeks were enrolled in a study that was conducted at five centers. They were treated with either loratadine or cetirizine 10mg daily in a single dose for 4 weeks. Exclusion criteria were a history of asthma, other systemic conditions that could interfere with the study, multiple drug allergies, known non-response to antihistamines, patients suffering from pressure urticaria or cold urticaria and women who were pregnant, nursing or using birth control pills. Also excluded were patients who had taken antihistamines for 72 hours, systemic corticosteroids for 1 month, topical steroids for 2 weeks, cromolyn for 2 weeks and decongestants for one day preceding the trial.

A general and systemic examination was conducted at the initial visit and an informed consent obtained. Physicians and patients evaluated the number of lesions and episodes, the average size and duration of lesions, and the degree of pruritus on a 4 point scale (Table I). Laboratory investigations (complete blood count, blood chemistry panel and urinalysis) were also performed at baseline (day 0) and at the end of the trial (day 28).

The patients were re-evaluated on days 3, 7, 14 and 27 after the start of treatment (Table I). For each patient, the scores of the individual evaluation criteria were added to determine the total symptom score; the mean total symptom score for each group was calculated likewise. The overall efficacy was assessed by the physician as either no improvement or worse, slight but insufficient improvement, definite improvement, and complete disappearance of signs and symptoms.

Table I: Rating scale for evaluation of severity of urticaria

No. of lesions	Score
0	0
1-10	1
11-20	2
>20	3
No. of episodes	**Score**
0	0
1	1
2	2
>3	3
Average size of lesions (inches)	**Score**
0	0
<0.5	1
0.5-1	2
>1	3
Duration of lesion(hrs)	**Score**
none	0
up to 4	1
>4-12	2
>12	3
Pruritus	**Score**
none	0
mild	1
mod	2
severe	3

Statistical analysis

Data from all centers were pooled for analysis. Variables of the two treatment groups such as sex, age, duration of disease and the entry level total symptom score were compared. Discrete variables were analysed by Fisher's Exact Test supplemented by categorical linear models. Continuous variables were analysed by a two-way analysis of variance extracting effects due to treatment, investigator and the treatment by investigator interactions. Variables, where appropriate, were used as grouping factors when analysing efficacy parameters.

Treatment group comparisons were performed on each parameter at each visit, via the two-way analysis of the variance model described above. An end point analysis was performed using the same model. The poolability of the multicentric data was evaluated by looking at the demographic information and the total symptom score.

Results

Of the 210 patients enrolled, eight dropped out for unknown reasons. Loratadine and cetirizine were given to 101 patients each. The two groups were similar in sex, age and weight.

The number, size and the duration of lesions showed a statistically significant improvement($p < 0.05$) in patients taking loratadine as compared to cetirizine at all visits. The number of episodes (Fig. 1) decreased in both the groups, and at the third, fourth and fifth visits there were significantly fewer episodes ($p < 0.05$) in the loratadine treated group.

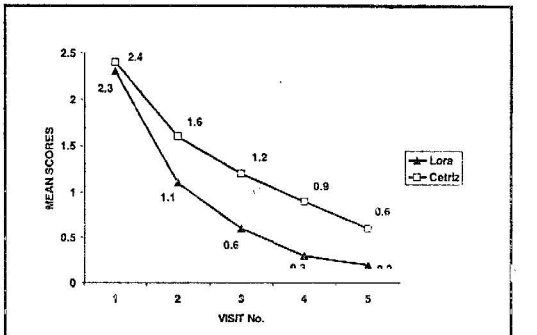

Fig.1:(Number of Lesions – Mean Scores Physicians Evaluations)

Fall in the mean score of pruritus was significantly ($p < 0.05$) greater with loratadine than with cetirizine. By the fourth visit, significantly more loratadine treated patients (Fig. 2) improved (81% vs 60%).

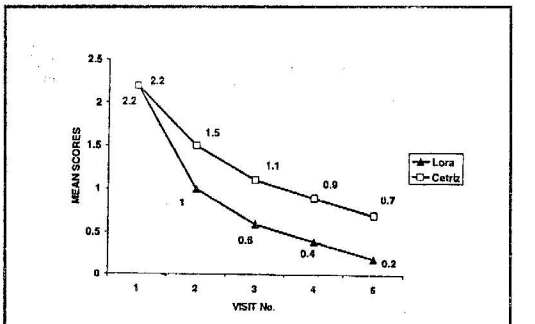

Fig.2:(Size of Lesions – Mean Scores Physicians Evaluations)

There were significantly ($p < 0.001$) fewer side effects (Table II) with loratadine (3%) than with cetirizine (21%).

Table II. Incidence of side effects

	Loratadine	Cetirizine
Dryness of mouth with sedation	2	7
Dryness of mouth alone	-	3
Sedation and drowsiness	2	10
Palpitation	1	-
Abdominal pain and loose motions	-	1
Headache	-	3

Discussion

This study showed that patients treated with loratadine had a significantly greater improvement than those treated with cetirizine. Adverse effects were much more common in the cetirizine treated group (21%) than in the loratadine treated group (3%), with 10 patients complaining of sedation in the cetirizine arm compared with only 2 in the loratadine arm.

Very little data is available comparing loratadine and cetirizine in urticaria. A study conducted by Guerra et al[9] on 116 patients also found that loratadine had a more rapid onset of action (3 days) than cetirizine. By day 14 and through the completion of the study, loratadine remained more effective than cetirizine in controlling urticarial symptoms. They also observed sedation to be more common with cetirizine (27%) than with loratadine (16%) [9].

A double-blind study in atopic dermatitis found both drugs to be well tolerated, though somnolence occurred more commonly with cetirizine(9%) than with loratadine(3%)[10]. A similar study in seasonal allergic rhinitis by Herman et al[12] observed that though both drugs were equally effective, cetirizine produced more drowsiness. Of 55 patients taking cetirizine, 11 patients developed drowsiness, 4 exhibited severe drowsiness, the intensity of which was never observed in the patients treated with loratadine. Of 53 patients taking loratadine, 7 patients developed drowsiness, 6 of minor, and 1 of moderate degree. [11]

Thus, it is seen that unlike loratadine, cetirizine, though less sedating than the first generation antihistamines, does not fit into the second generation non-sedating category. Loratadine is generally viewed as a safe and well tolerated medication in all ages and,unlike some other second generation antihistamines, does not produce sedation, cardiac toxicity or weight gain.

Conclusion

Loratadine satisfies the criteria for the ideal H1-antagonist for regular prophylactic treatment of urticaria[12]. It is orally active, has a rapid onset of action, requires once daily administration, and has minimal unwanted side effects. Its clinical effectiveness, combined with its selectivity, safety and tolerability, distinguished it from other members of its class, and makes it the most effective second generation antihistamine available for the treatment of urticaria.

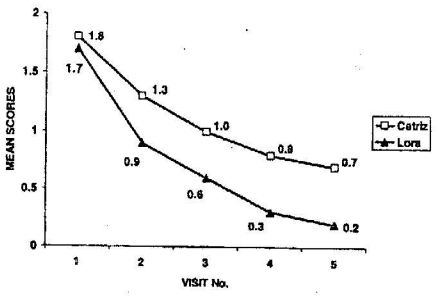

Fig. 3: (Duration of lesions – mean scores physicians evaluation)

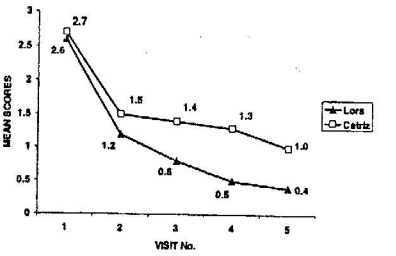

Fig. 4: (Number of Episodes – Mean Scores Physicians Evaluation)

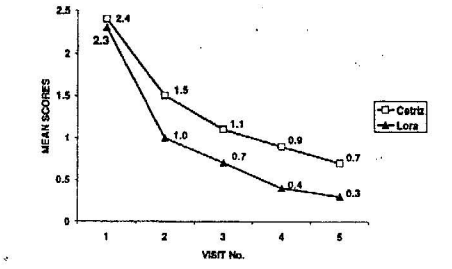

Fig. 5: (Pruritis – Mean Scores Physicians Evaluation)

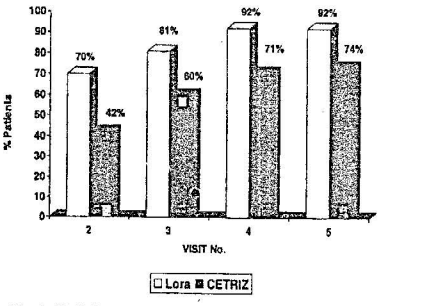

Fig. 6: (Definite Improvement (% Pts) Physicians Evaluation)

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