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A NEW ANTIHISTAMINE HC 20-511* COMPARED WITH DIMETINDEN (FENISTIL RETARD®) IN THE TREATMENT OF CHRONIC URTICARIA AND OTHER PRURITIC DERMATOSES

By

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When investigating the clinical efficacy of antihistaminic drugs, one uses patient groups with either allergic respiratory diseases or allergic and pruritic dermatoses. Among the dermatoses, the effectiveness of an antihistamine drug can best and most reliably be demonstrated in chronic urticaria (5).

Dimetinden (Fenistil) or dimethpyrindene maleate is an antihistamine, which has been on the market for over 10 years, and has been widely used in many countries. Its therapeutic effect has been confirmed in clinical trials (1, 2, 3).

The new antihistamine, HC 20-511, is the hydrogen fumarate of 4-(1-methyl-4-piperidylidene)-4H-benzo[4,5] cyclohepta[1,2-b]thiophene-10 (9H)-one (Fig. 1).

Preliminary pharmacological, toxicological, and clinical trials have shown HC 20-511 to be a fast-acting, effective, and safe drug. No teratological effects have been found in studies carried out on rats and rabbits (4).

The objectives of this study were to compare the therapeutic strength, the time until onset and duration of activity, as

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* Sandoz

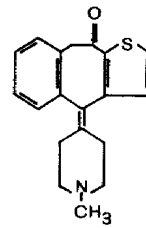

Fig. 1.
Structural formula of HC 20-511.

well as the tolerance of HC 20-511 and Dimetinden in chronic urticaria and some other chronic dermatoses.

PATIENTS AND METHODS

A total of 42 ambulatory patients (12 males and 30 females) were admitted to the study. The age of the patients varied between 14 and 73 years, the mean age being approximately 40 years.

The study included 28 patients suffering from urticaria. Of these, one patient suffered from heat-urticaria, another from cold-urticaria, and the remaining patients from chronic urticaria. The skin manifestations had been present for at least 2 months—in one patient for 26 years.

In the group consisting of other dermatoses, there were 14 patients, who were distributed, according to their diagnoses, as follows: *atopic eczema* (prurigo Besnier), 5 cases; *neurodermatitis circumscripta,* 2 cases; *pruritus sine materia,* 3 cases; and *lichen ruber planus,* 2 cases.

In a single-blind, comparative study, 22 patients received HC 20-511 and 20 patients Dimetinden (Fenistil retard). The reason for not performing the study double-blind was that the original Fenistil retard coated tablets had to be used in order not to lose the retard effect, while HC 20-511 was available only as capsules. The dosages were: HC 20-511 1 mg twice daily, and Dimetinden 2.5 mg twice daily. It was planned to continue the treatment for 4 weeks.

Before the beginning of the treatment, the symptoms and the dermatological state of the patients were recorded. Blood pressure, pulse rate, length, and weight were measured, and the following laboratory tests were performed: hemoglobin, leucocytes, eosinophiles, and erythrocyte sedimentation rate.

The clinical controls were performed after 7, 14, 21 and 28 days. At each control, all the above-mentioned symptoms and values were recorded, except for the laboratory tests, which were repeated only at the last control.

In the urticaria patients, the symptoms followed were: pruritus, erythema,

TABLE 1

Comparison of Efficacy, Tolerance, Onset and Duration of Effect of HC 20-511 and Dimetinden.

	HC 20-511		Dimetinden	
Efficacy				
– very effective	2	(59%)	1	(45%)
– effective	11		8	
– moderate—slight	6		3	
– no effect	3	(14%)	8	(40%)
Tolerance				
– excellent	9	(91%)	8	(85%)
– good	11		9	
– satisfactory	2		1	
– poor	0	(0%)	2	(10%)
Onset of effect				
– quick	13	(72%)	10	(63%)
– slow	5		6	
Duration of effect				
– long (8–12 h)	7	(39%)	6	(38%)
– moderate (4–8 h)	7		6	
– short (<4 h)	4		4	

and papules. In the other dermatoses erythema, scratch marks, lichenification, and the extent of skin changes were followed.

During the study the patients did not receive internally any cortisone, any other antihistamines, any calcium or any other antipruritic drugs. Local steroid treatment was also reduced to a minimum.

At each control, attention was paid to any side effects that had appeared.

RESULTS

The results are shown in Tables 1 and 2. When the whole material of 42 patients was considered, HC 20-511 was found to be clearly more effective than Dimetinden (Table 1). HC 20-511 was very effective or effective in 13 (59 per cent) and Dimetinden correspondingly in 9 patients (45 per cent). The difference is not statistically significant. On the other

TABLE 2

Efficacy of HC 20-511 and Dimetinden Retard in Chronic Urticaria.

	HC 20-511		Dimetinden	
Very good	2	(63%)	–	
Good	8		5	(42%)
Moderate	4		3	
Poor	2	(12%)	4	(33%)

hand, HC 20-511 was without effect in only three cases (14 per cent), while Dimetinden was so in eight cases (40 per cent). This difference is statistically significant.

The effect of HC 20-511 appeared more quickly than that of Dimetinden; the duration of the effect was the same for both preparations (Table 1).

When analyzing only the urticaria-group (Table 2), HC 20-511 is found to have been specially effective in these patients. When following the effect of the drug on the urticaria-symptoms (pruritis, erythema, papules) in the patients in the HC 20-511 group, a highly significant improvement ($P < 0.001$) was found as early as the first week of treatment (Fig. 2). In the patients in the Dimetinden group, however, this level of significance was not reached by any symptom during the whole time of treatment.

In the group consisting of other dermatoses, HC 20-511 and Dimetinden proved to have an almost equal antipruritic effect.

Side Effects

The tolerance of both antihistamines was generally good (Table 1). In the patients, who received Dimetinden, however, the adverse reactions which appeared were more numerous and more severe than in those treated with HC 20-511.

The most common side effect, as is generally found with antihistamines, was sedation, which appeared in approximately 50 per cent of patients in each group. The sedation

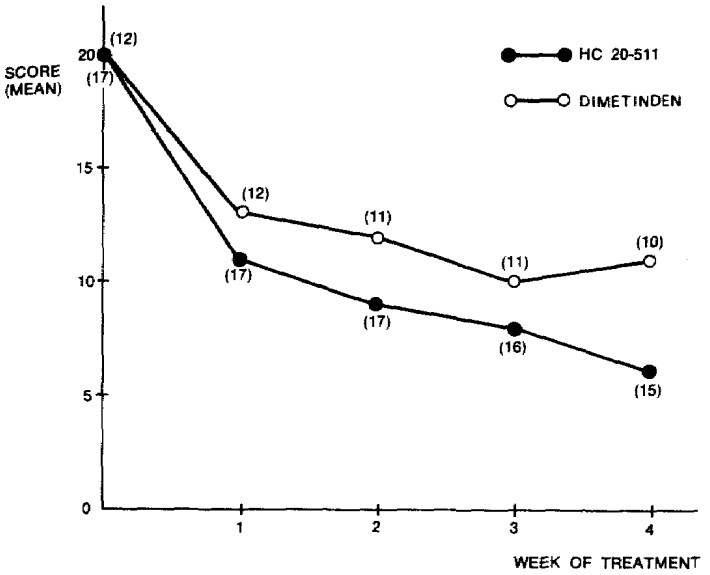

Fig. 2.
Urticaria. Mean score of the symptoms (erythema, papules and pruritus) during treatment. Number of patients in brackets.

troubling the patients at the beginning of treatment disappeared, however, in almost half of the patients in each group when the treatment continued.

In two patients on Dimetinden, the treatment had to be interrupted during the first week of treatment due to severe side effects. In these patients vomiting, dizziness, fainting, and extreme tiredness appeared. Both patients were then treated with HC 20-511, which was well tolerated. Three patients discontinued the treatment after 3 weeks, primarily because of lack of effect. Of these, two received Dimetinden and one HC 20-511. One patient on HC 20-511 had to interrupt the treatment after 2 weeks as he fell ill with pneumonia. All the others continued the treatment for 4 weeks.

Neither of the drugs was found to have an increasing or

decreasing effect on blood pressure, pulse rate or weight. Neither could any significant changes of the hemoglobin-, leucocyte-, eosinophile- or ESR-values be found.

DISCUSSION

Søbye & Ulrich (5) compared Dimetinden with Clemastine in patients suffering from chronic urticaria, and demonstrated Clemastine to be more effective (5). The pharmacological and preliminary clinical experiments done with HC 20-511 showed this antihistamine to be faster acting and more effective than Clemastine when equal doses are compared (4).

The present clinical trial in 28 patients suffering from urticaria demonstrates HC 20-511 to be clearly more effective than Dimetinden in chronic urticaria.

The effect of HC 20-511, which is not a retard-preparation, appeared somewhat faster than that of Dimetinden, and the duration of the effect was as long as that of Dimetinden, although the latter was given in the retard-form as tablets of 2.5 mg.

SUMMARY

The new antihistamine, HC 20-511 (Sandoz), was compared with Dimetinden (Fenistil retard®) in a single-blind comparative study in 42 patients with dermatoses, 28 of whom suffered from chronic urticaria.

HC 20-511 had a better effect, especially in chronic urticaria, where pruritus, erythema and papules quickly disappeared. The effect appeared somewhat faster than and lasted as long as that of Dimetinden, although HC 20-511 is not a retard-preparation unlike the Dimetinden preparation used for comparison. HC 20-511 also caused less side effects.

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