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COMPARISON OF
A NEW ANTIHISTAMINE HC 20-511* WITH
CYPROHEPTADINE (PERIACTIN®)
IN CHRONIC URTICARIA

By

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Preliminary investigations have shown that HC 20-511, the hydrogen fumarate of 4—(1-methyl-4-piperidylidene)—4H-benzo [4,5] cyclohepta [1,2-6] thiophene-10 (9H-one), is an effective, fast-acting and safe anti-allergic agent which also has anti-anaphylactic and antihistaminic properties (1,2).

Cyproheptadine (Periactin®) is a well-known and widely used histamine and serotonin antagonist (3,5).

The aim of the present study was to compare the effect and tolerance of cyproheptadine and HC 20-511 in chronic urticaria. HC 20-511 was given in two different dosages.

PATIENTS AND METHODS

The study was a clinical-therapeutic, double-blind study with parallel groups and randomized allocation of the medications.

Fifty patients suffering from urticaria, 31 women and 19 men, participated in the study. All patients were more than 18 years of age, the average age being 38 years. Two patients suffered from cold urticaria, the remaining from chronic urticaria of unknown cause. The skin manifestations had been present for at least 2 months, the mean duration of the diseases being 2½ years.

For 48 patients the treatment period comprised 4 weeks, and for one patient 2 weeks. One patient on Periactin was excluded from the study, because he interrupted treatment after 3 days due to acute prostatitis.

*) Manufactured by Sandoz Ltd., Basle, Switzerland.

There were two dosage forms of HC 20-511, i.e. capsules containing 1 mg and 2 mg active substance. Cyproheptadine was administered in capsules of 4 mg. The dosage was one capsule twice daily.

The final result was calculated from 49 patients who were divided into the following groups according to different dosages:

HC 20-511	2 mg/day - 16 patients
HC 20-511	4 mg/day - 16 patients
Cyproheptadine	8 mg/day - 17 patients

The patients were examined weekly during the time of the study and the objective symptoms—erythema and urticaria papules—recorded with scores. The effect and the tolerance of the drug was followed, as well as possible side effects, such as sedation, dryness of the mouth and dizziness. At each control, weight, blood pressure and pulse rate were measured. Finally, a global assessment of efficacy, tolerance and side effects was made for each patient at the end of the study.

Additionally, the patients kept a daily record of their symptoms such as itching, etc. and finally evaluated the onset and duration of effect.

RESULTS

According to the statistical analysis all three patient groups were homogenous regarding sex, age, weight, height and duration of urticaria.

In all three groups erythema and urticaria papules decreased statistically significantly throughout the study from the first control. HC 20-511 in daily doses of 4 mg and cyproheptadine were almost equally effective and HC 20-511, in daily doses of 2 mg, somewhat weaker when evaluated with the mean scores of the objective symptoms. No statistically significant differences could be detected between the groups.

According to the global evaluation of the physician (Table 1), HC 20-511 in daily doses of 4 mg was the most effective in urticaria. In this group a very good result was achieved in 75 % of the cases. Cyproheptadine was almost as good (71 %), and HC 20-511 in daily doses of 2 mg had the weakest effect (50 %).

In both HC 20-511-groups there were three patients and

in the cyproheptadine-group two, on whom the drug had a poor effect.

TABLE 1

Comparison of HC 20-511, 2 mg and 4 mg Daily, and Cyproheptadine 8 mg Daily with Regard to Efficacy, Tolerance, Sedation, Onset and Duration.

Physicians' evaluation 49 cases	HC 20-511 2 mg/day	HC 20-511 4 mg/day	Cyproheptadine 8 mg/day
<i>Efficacy</i>			
very effective	—	—	—
effective	8 (50 %)	12 (75 %)	12 (71 %)
moderate	5	1	3
poor	3	3	2
<i>Tolerance</i>			
very good	—	—	—
good	15 (94 %)	14 (88 %)	13 (77 %)
moderate	1	2	2
poor	—	—	2
<i>Sedation</i>			
mild	3	4	6
strong	1	3	3
unacceptable	—	—	1
Patients' evaluation 39 cases			
<i>Onset of effect</i>			
quick (< 1 h)	6 (46 %)	11 (85 %)	6 (46 %)
slow (> 1 h)	7	2	7
<i>Duration of effect</i>			
long (> 8 h)	7 (54 %)	11 (85 %)	7 (54 %)
moderate (4—8 h)	2	—	6
short (< 4 h)	4	2	—

The patients' own evaluation was obtained from the cards of 13 patients in each group (39 in all). On the average, itching began to disappear on the third day of treatment for those on daily doses of 2 mg HC 20-511, and on the second day for the others. The fastest onset of effect was

apparent with HC 20-511 in daily doses of 4 mg. Table 1 shows that the effect began in less than 1 h in 85 % of the patients in this group. In the other two groups the effect began in less than 1 h in 46 %, and took longer, i.e. more than 8 h, in 54 %. The daily doses of 4 mg HC 20-511 proved also to be most long-lasting, because in 85 % the effect lasted longer than 8 h.

Table 1 also shows that in 21 patients the drug acted as a sedative. Of these, four had received HC 20-511 2 mg daily, and seven 4 mg daily. Ten patients on cyproheptadine suffered from tiredness. Of these, one patient had to interrupt the treatment after 2 weeks due to its sedative effect, two more patients suffered from severe tiredness during the first 2 weeks of treatment. However, this diminished substantially during the third and fourth week. None of the patients had dryness of the mouth or dizziness.

Two patients on daily doses of 4 mg HC 20-511 reported increased appetite during the study. A follow-up of weight showed that in this group 12 patients had increased weight, on an average of 1.5 kg. Thirteen patients in the cyproheptadine group showed on average a weight increase of 1.2 kg. However, the patients on HC 20-511 2 mg daily showed no significant increase of weight. Blood pressure and pulse rate values remained unchanged throughout the study.

DISCUSSION

In previously performed clinical studies HC 20-511 proved to be more effective than dimetinden in the treatment of urticaria (4).

In this study 4 mg HC 20-511 daily was slightly more effective than 8 mg cyproheptadine daily but doses of 2 mg HC 20-511 daily were clearly less effective.

On the other hand, there was better tolerance with HC 20-511 and less sedative effect with HC 20-511 than with cyproheptadine. A great disadvantage of HC 20-511 was the appetite stimulating effect, with consequent weight increase,

which resulted with daily doses of 4 mg, but not in doses of 2 mg HC 20-511. The same disadvantage was noted with cyproheptadine in daily doses of 8 mg.

SUMMARY

The effect and tolerance of a new antihistamine, HC 20-511, in daily doses of 2 and 4 mg was compared with cyproheptadine (Periactin) 8 mg daily in 50 cases of chronic urticaria.

HC 20-511 4 mg daily proved to be the most effective, rapid and long-lasting. HC 20-511 had less sedative effect than cyproheptadine, but both possessed the same appetite-stimulating effect. However, this was not noted with the smaller dosage of HC 20-511.

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