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# Clinical investigation of ketotifen in perennial allergic rhinitis: A double-blind comparative study of ketotifen and clemastine fumarate

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SUMMARY

*In several clinics we carried out a comparative double-blind study of ketotifen (HC) in 260 patients with perennial rhinitis in order to reveal the clinical efficacy, safety and usefulness. We administered two different doses of HC (0.5 mg × 2 and 1 mg × 2 daily), clemastine fumarate, CF (1.34 mg × 2 daily) and their placebos. The active drugs were always given in combination with their placebos during a period of 4 weeks. The results indicated that HC, especially HC 1 mg × 2, was superior to CF in efficacy and usefulness. Side-effects were mild and the frequency in which they occurred was similar to CF. In contrast to CF, HC showed an efficacy not only in sneezing and nasal discharge but also in nasal obstruction as well.*

## INTRODUCTION

Since ketotifen (HC) possesses antihistaminic and anti-allergic properties which inhibit the release of histamine and SRS-A from rat peritoneal mast cells and also causes fewer side-effects (Kumagai and Tomioka, 1978; Martin and Römer, 1978; Martin and Baggiolini, 1981; Oka et al., 1979; Tomioka et al., 1979), it has been widely used for patients with allergic rhinitis and bronchial asthma in Europe. However, as far as we know, only 2-3 data of a detailed investigation on its efficacy, safety and usefulness in allergic rhinitis have been reported (Davies, 1982; Horak and Hussarek, 1977; Warner and Goldsworthy, 1982). Therefore, we carried out a comparative double-blind study of ketotifen and clemastine fumarate (hereafter abbreviated as CF) in patients with perennial nasal allergy in several clinics.

## METHOD

### *1. Subject*

Two hundred and sixty patients having perennial allergic rhinitis were selected for the present study by the following criteria.

1. Twelve years of age and older.

2. Two or more tests such as a skin reaction by antigen, a nasal provocation reaction and an increase of eosinophils in the nasal discharge are positive.
3. No complication of severe nasal diseases other than allergic rhinitis.
4. The expectation is that a use of other anti-allergy drugs can be avoided during the test period.

*2. Test drug and the method of administering*

A white capsule containing two different doses of HC and their placebo (hereafter abbreviated as P) and a white tablet containing CF 1.34 mg and its placebo were orally administered twice a day for four successive weeks. The dosage given was divided as follows:

1. HC 0.5 mg + CF placebo (HC 0.5-group)
2. HC 1.0 mg + CF placebo (HC 1.0-group)
3. HC placebo + CF 1.34 mg (CF-group).

*3. Investigation and test methods*

Since the allergy test method, the classification of the degree and the severity of nasal symptoms and the classification of local findings have already been reported (Okuda et al., 1983), we did not mention these items in this report. Investigation of the subjective symptoms was done by studying the patient's case history and by their allergy diary.

The test schedule is as follows:

After the selection of the subjects on account of their case history, allergy test, general laboratory examinations, and allergic rhinitis diary, the pre-treatment observation period was set for one week. Symptoms and objective findings during this period were recorded in the diary and case card. Then, HC 0.5 mg, HC 1.0 mg and CF were administered for four weeks. Immediately after the termination of this period of administration, the general laboratory examinations and the collection of the test drugs were recorded in the case card.

After the follow-up period (no drugs administered) which was set for one week, a collection was made of the allergy diary and a record was made of the case card.

*4. Assessment of efficacy*

The assessment to what extent improvement occurred was defined by the impression of the physician in charge according to five classes (markedly effective, effective, slightly effective, ineffective, aggravated).

Judgement of the efficacy was made by the occurrence of the symptoms according to five classes (disappearance, marked improvement, improvement, no change, aggravation).

The overall safety was defined according to four classes (none, mild, moderate, severe).

The overall usefulness was assessed according to five classes (very useful, useful, slightly useful, useless, harmful). The change in the nasal symptoms during the follow-up period was determined according to three classes (improved, unchanged, aggravated).
The frequency of sneezing attacks and the frequency of blowing of the nose was totalled every two weeks in accordance with the allergic rhinitis diary. Scores were given to indicate the degree of nasal obstruction ( + : 1, + + : 2, + + + : 3). These scores were totalled every two weeks and a comparison was made between the control period, the treatment period and the follow-up period.
The side-effects were investigated by means of studying the case histories and inspection of the physician in charge. Also, the results of general laboratory examinations, carried out before and after the period of administration, were compared.

*5. Statistical analysis*
The differences among the three groups were compared by means of several tests (H-test, $x^2$-test, analysis of variance). As for the cases in which significant difference was observed, further comparisons were made between the two groups (U-test, Fisher's Direct Probability Estimate). Paired t-test was used for group comparison.

## RESULTS

*1. Subjects*
The total number of cases investigated was 260 (HC 1.0 : 87, HC 0.5 : 89, CF : 84), of whom 39 dropped out and the remaining 221 cases (HC 1.0 : 74, HC 0.5 : 74, CF : 73) were used for analysis. As for the background factors of the patients involved in the analysis, no significant difference was observed among the three groups (HC 1.0, HC 0.5, CF) in any of the items including age, sex, complications, major causal antigen, combined causal antigen, severity of symptoms, type of disease, season of predilection, age of onset of illness, period of affection, history of atopic disease and history of treatment. The rate of drug-intake in HC 0.5-group was 76% or more for both capsule and tablet, showing a tendency of higher rate than the CF-group (U-test: $p < 0.05$).
No significant difference was observed between the three groups as far as the following factors are concerned, frequency of sneezing attacks, nasal discharge, nasal obstruction, olfactory disturbance, discomfort in daily life, swelling and colour of the nasal mucous membrane, the amount of watery secretion, nasal provocation reaction and the number of eosinophils in the nasal discharge during the control period. However, as for the property of the nasal discharge, watery discharge was more frequently found in the CF-group (U-test: $p < 0.05$).

*2. Global improvement rate*

The degree of improvement which could be defined as "effective" and "markedly effective" was 72.7% in the HC 1.0-group, 54.9% in the HC 0.5-group and 34.7% in the CF-group. The results of the HC-group (1.0 and 0.5) were significantly higher than the one of the CF group (U-test: $p < 0.001$, $p < 0.01$, Fisher: $p < 0.001$, $p < 0.05$). The rate of efficacy in the HC 1.0-group was higher than that of the HC 0.5-group, being indicative of a tendency to respond to the given dose (Fisher: $p < 0.05$) (Table 1).

Table 1. Global improvement rating (Judgement by physician).

| drug | no. of cases | markedly effective | effective | slightly effective | ineffective | aggravated | H-test U-test | effective and markedly effective (%) | $\chi^2$-test Fisher |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | $p = 0.0000$ | | $p = 0.0007$ |
| HC 1.0 | 66 | 12 | 36 | 9 | 9 | 0 | HC 1.0 > CF*** | 72.7 | HC 1.0 > HC 0.5* |
| HC 0.5 | 71 | 7 | 32 | 24 | 7 | 1 | HC 0.5 > CF** | 54.9 | HC 1.0 > CF*** |
| CF | 72 | 5 | 20 | 15 | 32 | 0 | | 34.7 | HC 0.5 > CF* |

*: $p < 0.05$ **: $p < 0.01$ ***: $p < 0.001$

*3. Efficacy on the symptoms*

In comparison with the control period, the HC 1.0-group showed "improvement" and "marked improvement" during the period of treatment for the following symptoms: sneezing attacks (71.2%), nasal discharge (65.6%), nasal obstruction at the time of the attack (62.7%), nasal obstruction in the ordinary state (56.3%), olfactory disturbance (57.1%), discomfort in daily life (75.6%), swelling of the nasal mucous membrane (56.1%), colour of the nasal mucosa (23.7%), the amount of watery nasal secretion (62.7%), property of nasal secretion (32.2%), the degree of nasal provocation reaction (76.5%), and the number of eosinophils in nasal discharge (54.8%). Significant differences were observed in sneezing attacks (Fisher: $p < 0.05$), nasal obstruction at the time of the attack (U-test: $p < 0.001$, Fisher: $p < 0.01$), nasal obstruction in the ordinary state (Fisher: $p < 0.05$), olfactory disturbances (Fisher: $p < 0.05$), discomfort in daily life (U-test: $p < 0.05$, Fisher: $p < 0.001$) between the CF-group and the HC 1.0-group.

In the HC 0.5-group, improvement was observed in sneezing attacks (62.7%), nasal discharge (50.8%), nasal obstruction (57.1% at the time of the attack and

Table 2.1. Efficacy on the symptoms (Comparison of control period and treatment period).

| symptoms | | drug | no. of cases | disappearance | marked improvement | improvement | no change | aggravation | no symptoms # | H-test U-test | marked improvement and disappearance (%) | improvement and marked improvement (%) | $\chi^2$-test Fisher "improvement" or better |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| nasal symptoms | sneezing attacks | HC 1.0 | 62 | 21(35.6) | 3(5.1) | 18(30.5) | 16(27.1) | 1( 1.7) | 3 | | 40.7 | 71.2 | $p = 0.0701$ |
| | | HC 0.5 | 67 | 17(25.4) | 5(7.5) | 20(29.9) | 24(35.8) | 1( 1.5) | 0 | N.S. | 32.8 | 62.7 | HC 1.0 > CF* |
| | | CF | 63 | 15(24.6) | 2(3.3) | 14(23.0) | 29(47.5) | 1( 1.6) | 2 | | 27.9 | 50.8 | |
| | nasal discharge | HC 1.0 | 62 | 16(26.2) | 5(8.2) | 19(31.2) | 21(34.4) | 0 | 1 | $p = 0.0709$ | 34.4 | 65.6 | |
| | | HC 0.5 | 66 | 9(14.3) | 5(7.9) | 18(28.6) | 25(39.7) | 6( 9.5) | 3 | HC 1.0 > HC 0.5$^+$ | 22.2 | 50.8 | N.S. |
| | | CF | 63 | 8(12.9) | 5(8.1) | 23(37.1) | 25(40.3) | 1( 1.6) | 1 | | 21.0 | 58.1 | |
| | nasal obstruction (at attack) | HC 1.0 | 62 | 22(37.3) | 4(6.8) | 11(18.6) | 18(30.5) | 4( 6.8) | 3 | $p = 0.0002$ | 44.1 | 62.7 | $p = 0.0022$ |
| | | HC 0.5 | 67 | 18(28.6) | 4(6.4) | 14(22.2) | 25(39.7) | 2( 3.2) | 4 | HC 1.0 > CF*** | 34.9 | 57.1 | HC 1.0 > CF** |
| | | CF | 62 | 9(14.8) | 1(1.6) | 10(16.4) | 27(44.3) | 14(23.0) | 1 | HC 0.5 > CF** | 16.4 | 32.8 | HC 0.5 > CF** |
| | nasal obstruction (ordinary state) | HC 1.0 | 59 | 10(31.3) | 3(9.4) | 5(15.6) | 8(25.0) | 6(18.8) | 27 | $p = 0.0098$ | 40.6 | 56.3 | $p = 0.0093$ |
| | | HC 0.5 | 67 | 15(31.9) | 1(2.1) | 10(21.3) | 16(34.0) | 5(10.6) | 20 | HC 1.0 > CF$^+$ | 34.0 | 55.3 | HC 1.0 > CF* |
| | | CF | 61 | 6(12.8) | 1(2.1) | 6(12.8) | 22(46.8) | 12(25.5) | 14 | HC 0.5 > CF* | 14.9 | 27.7 | HC 0.5 > CF* |
| | olfactory disturbance | HC 1.0 | 59 | 10(35.7) | 1(3.6) | 5(17.9) | 10(35.7) | 2( 7.1) | 31 | | 39.3 | 57.1 | $p = 0.0467$ |
| | | HC 0.5 | 63 | 12(36.4) | 0 | 6(18.2) | 12(36.4) | 3( 9.1) | 30 | N.S. | 36.4 | 54.5 | HC 1.0 > CF* |
| | | CF | 59 | 7(20.6) | 1(2.9) | 2( 5.9) | 22(64.7) | 2( 5.9) | 25 | | 23.5 | 29.4 | HC 0.5 > CF* |
| | discomfort in daily life | HC 1.0 | 59 | 20(44.4) | 0 | 14(31.1) | 9(20.0) | 2( 4.4) | 14 | $p = 0.0256$ | 44.4 | 75.6 | $p = 0.0030$ |
| | | HC 0.5 | 64 | 14(30.4) | 2(4.4) | 10(21.7) | 16(34.8) | 4( 8.7) | 18 | HC 1.0 > CF* | 34.8 | 56.5 | HC1.0 > HC0.5$^+$ |
| | | CF | 61 | 12(25.5) | 2(4.3) | 5(10.6) | 26(55.3) | 2( 4.3) | 14 | | 29.8 | 40.4 | HC1.0 > CF*** |

+: $p < 0.10$ *: $p < 0.05$ **: $p < 0.01$ ***: $p < 0.001$ #: %, not included in the tests ( ): %

Table 2.2. Efficacy on the symptoms (Comparison of control period and treatment period).

| symptoms | | drug | no. of cases | disappearance | marked improvement | improvement | no change | aggravation | no. symptoms # | H-test U-test | marked improvement and disappearance (%) | improvement and marked improvement (%) | $\chi^2$-test Fisher "improvement" or better |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| nasal findings | swelling | HC 1.0 | 60 | 8(14.0) | 6(10.5) | 18(31.6) | 22(38.6) | 3( 5.3) | 3 | | 24.6 | 56.1 | |
| | | HC 0.5 | 61 | 13(23.2) | 2( 3.6) | 19(33.9) | 20(35.7) | 2( 3.6) | 5 | N.S. | 26.8 | 60.7 | N.S. |
| | | CF | 53 | 5(10.0) | 2( 4.0) | 25(50.0) | 16(32.0) | 2( 4.0) | 3 | | 14.0 | 64.0 | |
| | colour of mucous membrane | HC 1.0 | 60 | 7(11.9) | 5( 8.5) | 2( 3.4) | 41(69.5) | 4( 6.8) | 1 | | 20.3 | 23.7 | |
| | | HC 0.5 | 63 | 7(11.5) | 6( 9.8) | 4( 6.6) | 42(68.9) | 2( 3.3) | 2 | N.S. | 21.3 | 27.9 | N.S. |
| | | CF | 59 | 6(10.2) | 5( 8.5) | 2( 3.4) | 41(69.5) | 5( 8.5) | 0 | | 18.6 | 22.0 | |
| | watery nasal discharge | HC 1.0 | 61 | 19(32.2) | 1( 1.7) | 17(28.8) | 18(30.5) | 4( 6.8) | 2 | | 33.9 | 62.7 | |
| | | HC 0.5 | 62 | 14(25.9) | 4( 7.4) | 8(14.8) | 26(48.2) | 2( 3.7) | 8 | N.S. | 33.3 | 48.1 | N.S. |
| | | CF | 57 | 13(24.1) | 1( 1.9) | 13(24.1) | 24(44.4) | 3( 5.6) | 3 | | 25.9 | 50.0 | |
| | property of nasal discharge | HC 1.0 | 61 | 16(27.1) | 0 | 3( 5.1) | 36(61.0) | 4( 6.8) | 2 | | 27.1 | 32.2 | |
| | | HC 0.5 | 63 | 11(19.6) | 0 | 8(14.3) | 36(64.3) | 1( 1.8) | 7 | N.S. | 19.6 | 33.9 | N.S. |
| | | CF | 56 | 15(26.8) | 0 | 3( 5.4) | 36(64.3) | 2( 3.6) | 0 | | 26.8 | 32.1 | |
| | nasal provocation reaction | HC 1.0 | 35 | 14(41.2) | 2( 5.9) | 10(29.4) | 7(20.6) | 1( 2.9) | 1 | | 47.1 | 76.5 | |
| | | HC 0.5 | 37 | 10(37.0) | 3(11.1) | 8(29.6) | 5(18.5) | 1( 3.7) | 10 | N.S. | 48.1 | 77.8 | N.S. |
| | | CF | 31 | 9(36.0) | 2( 8.0) | 7(28.0) | 6(24.0) | 1( 4.0) | 6 | | 44.0 | 72.0 | |
| | no. of eosinophils in nasal discharge | HC 1.0 | 42 | 13(31.0) | 2( 4.8) | 8(19.1) | 14(33.3) | 5(11.9) | 0 | | 35.7 | 54.8 | |
| | | HC 0.5 | 42 | 6(15.4) | 2( 5.1) | 12(30.8) | 17(43.6) | 2( 5.1) | 3 | N.S. | 20.5 | 51.3 | N.S. |
| | | CF | 37 | 5(14.7) | 0 | 10(29.4) | 15(44.1) | 4(11.8) | 3 | | 14.7 | 44.1 | |

# : %, not included in the tests ( ): %

55.3% in the ordinary state), olfactory disturbances (54.5%), discomfort in daily life (56.5%), swelling (60.7%), colour (27.9%), watery secretion (48.1%), property of nasal secretion (33.9%), nasal provocation reaction (77.8%), the number of eosinophils in the nasal discharge (51.3%). Significant differences were observed between the CF-group and the HC 0.5-group in nasal obstruction and olfactory disturbances only (Table 2.1 and 2.2).

*4. Overall safety*

The occurrence of side-effects was 27.0% in the HC 1.0-group, 20.3% in the HC 0.5-group and 26.0% in the CF-group. There was no significant difference among the 3 groups (H-test, $x^2$-test) (Table 3).

Table 3. Overall safety rating (Judgement by physician).

| drug | no. of cases | severe | moderate | mild | none | H-test | $\chi^2$-test ("severe"~ "mild"/none) |
|---|---|---|---|---|---|---|---|
| HC 1.0 | 74 | 3 | 5 | 12 | 54 | N.S. | N.S. |
| | | 20 (27.0%) | | | | | |
| HC 0.5 | 74 | 2 | 2 | 11 | 59 | | |
| | | 15 (20.3%) | | | | | |
| CF | 73 | 0 | 4 | 15 | 54 | | |
| | | 19 (26.0%) | | | | | |

*5. Overall usefulness*

Cases which could be defined as "useful" and "very useful" occurred for 64.9% in the HC-group, 47.3% in the HC 0.5-group and 35.6% in the CF-group. The HC 1.0-

Table 4. Overall usefulness (Judgement by physician).

| drug | no. of cases | very useful | useful | slightly useful | useless | harmful | H-test U-test | useful and very useful (%) | $\chi^2$-test Fisher |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | $p = 0.0003$ | | $p = 0.0017$ |
| HC 1.0 | 74 | 11 | 37 | 10 | 16 | 0 | HC 1.0 > CF*** | 64.9 | HC 1.0 > HC 0.5* |
| HC 0.5 | 74 | 7 | 28 | 28 | 8 | 3 | HC 0.5 > CF* | 47.3 | HC 1.0 > CF*** |
| CF | 73 | 3 | 23 | 14 | 31 | 2 | | 35.6 | |

*: $p < 0.05$ ***: $p < 0.001$

group showing significantly higher usefulness than the CF-group (U-test: $p < 0.001$, Fisher: $p < 0.001$). The HC 0.5-group was also significantly superior to the CF-group (U-test: $p < 0.05$). At the same time, the HC 1.0-group showed a significantly higher usefulness than the HC 0.5-group (Fisher: $p < 0.05$) (Table 4).

*6. Degree of nasal symptoms during the follow-up period*

In comparison with the control period, cases which could be defined as "improved" and "markedly improved" comprise 60.0% in the HC 1.0-group, 63.9% in the HC 0.5-group and 63.2% in the CF-group. There were no significant differences among the three groups. In comparison with the treatment period, those which could be defined as "improved" and "markedly improved" were 10.0%, 18.0%, 8.8% respectively. There were also no significant differences among the three groups (Table 5).

Table 5. Assessment of nasal symptoms during follow-up period (Judgement by physician).

| | drug | no. of cases | improved | unchanged | aggravated | H-test | improved and markedly improved (%) | $\chi^2$-test |
|---|---|---|---|---|---|---|---|---|
| in comparison with control period | HC 1.0 | 60 | 36 | 22 | 2 | N.S. | 60.0 | N.S. |
| | HC 0.5 | 61 | 39 | 19 | 3 | | 63.9 | |
| | CF | 57 | 36 | 18 | 3 | | 63.2 | |
| in comparison with treatment period | HC 1.0 | 60 | 6 | 24 | 30 | N.S. | 10.0 | N.S. |
| | HC 0.5 | 61 | 11 | 23 | 27 | | 18.0 | |
| | CF | 57 | 5 | 28 | 24 | | 8.8 | |

*7. Assessment of the efficacy in accordance with the allergic rhinitis diary*

The average daily frequency of sneezing attacks decreased significantly ($p < 0.001$) two weeks after drug administration in all three groups in comparison with the control period. In the fourth week, a tendency of further decrease was observed in comparison with the 2nd week. In the follow-up period, it increased, but did not return to the level of the control period (Figure 1).

The average daily frequency of blowing the nose showed a similar tendency of decrease as the sneezing attacks (Figure 2).

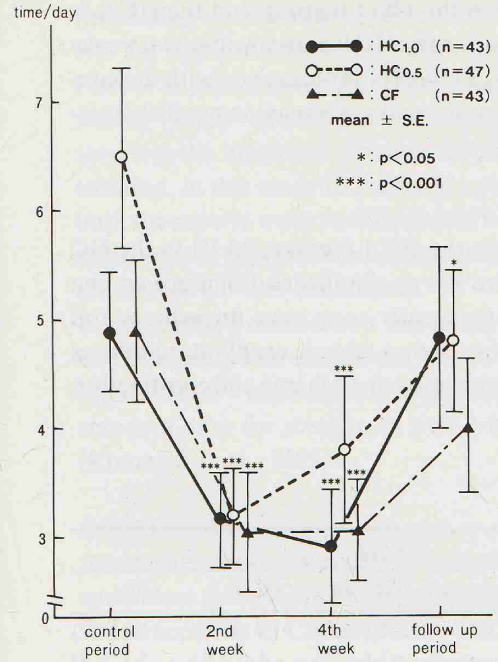


Figure 1.
Average frequency of sneezing attacks.

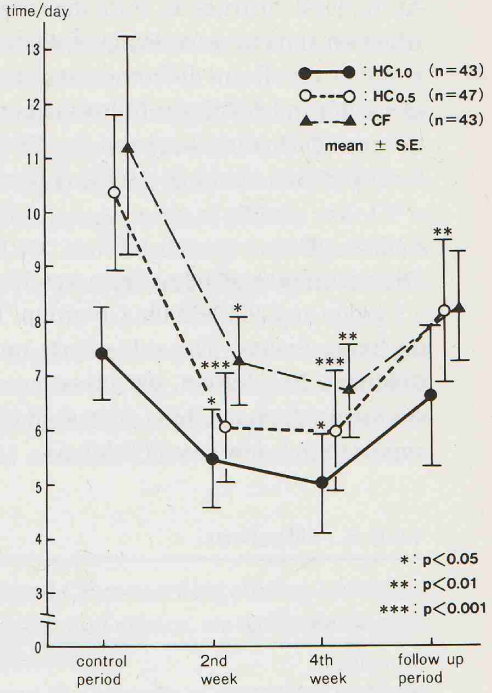


Figure 2.
Average frequency of blowing of the nose.

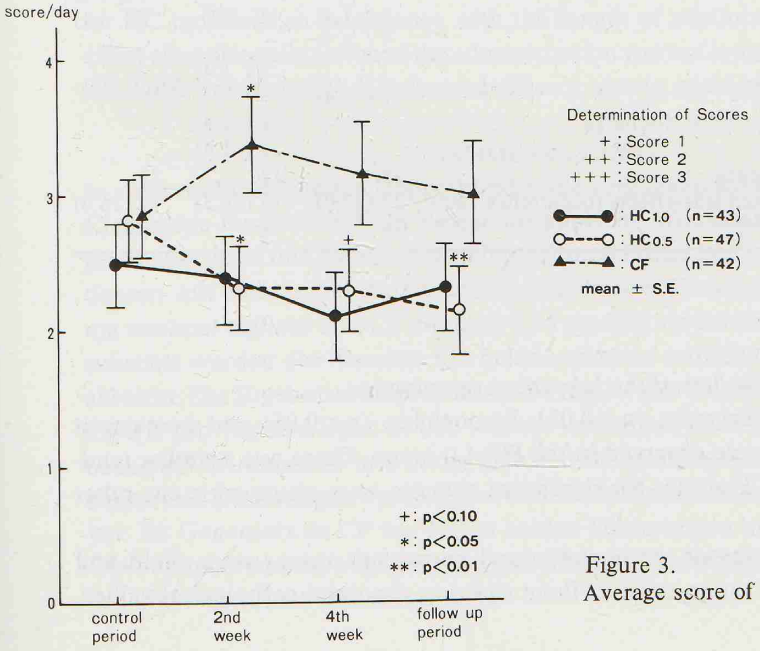


Figure 3.
Average score of nasal obstruction.

As for nasal obstruction, both the average daily scores used to indicate nasal obstruction showed a tendency of decrease in the HC 1.0-group and the HC 0.5-group. A significant difference was observed in the HC 0.5-group after two weeks ($p < 0.05$) and during the follow-up period ($p < 0.01$) in comparison with the control period. On the other hand, the CF-group showed an increase in nasal obstruction after two weeks ($p < 0.05$) (Figure 3).

*8. Side-effects*

The occurrence of side-effects was 27.0% in the HC 1.0-group, 20.3% in the HC 0.5-group and 26.0% in the CF-group. There was no significant difference among the three groups. The side-effects most frequently seen were drowsiness and tiredness. In addition, dizziness, heavy headaches, thirst, eruption, aphthous stomatitis, dermal itching, increased viscosity of nasal discharge and constipation appeared in a few cases (Table 6).

Table 6. Side-effects.

| | drug | | |
|---|---|---|---|
| type of side-effects | HC 1.0 | HC 0.5 | CF |
| drowsiness | 14 (18.9) | 13 (17.6) | 18 (24.7) |
| tiredness | 3 ( 4.1) | 4 ( 5.4) | 5 ( 6.8) |
| dizziness | 2 ( 2.7) | | |
| heavy headaches | 2 ( 2.7) | | 1 ( 1.4) |
| nausea | | | 1 ( 1.4) |
| dry mouth | 1 ( 1.4) | 2( 2.7) | 3 ( 4.1) |
| eruption | 2 ( 2.7) | | |
| aphthous stomatitis | | 1 ( 1.4) | |
| dermal itching | 1 ( 1.4) | | |
| increased viscosity of nasal discharge | | 1 ( 1.4) | |
| constipation | | 1 ( 1.4) | |
| frequency of occurrence | 28 | 22 | 28 |
| no. of cases manifested side-effects (occurrence rate) | 20 (27.0) | 15 (20.3) | 19 (26.0) |
| total no. of cases | 74 | 74 | 73 |

( ): %

*9. Changes in the values of the laboratory examination*

Decreases in erythrocytes ($p < 0.01$), hemoglobin ($p < 0.05$) and hematocrit values ($p < 0.01$) were observed in the HC 1.0-group. There was a similar tendency also in the CF-group. No significant changes were observed in the other items.

Changes in erythrocytes, hemoglobin and hematocrit values were slight and within the normal range, none of them showing abnormal pathological values.

## DISCUSSION

Interesting results were obtained from this comparative study of HC (especially HC 1.0 mg) and CF in perennial allergic rhinitis.

First of all, HC showed an efficacy superior to CF. Although Warner and Goldsworthy (1982) reported that difference in efficacy between HC and CF was observed in the long-term administration (50 days) but not in the short-term administration, in this study HC showed a significant superiority of efficacy over CF in both the second week and the fourth week. HC showed efficacy in all three major symptoms of allergic rhinitis, especially as for nasal obstruction in which case the efficacy of CF was insufficient.

In this study, a comparison was made for the dose of 1 mg × 2 and 0.5 mg × 2. As for the efficacy and usefulness, 2 mg was superior to 1 mg. Although Horak (1977) reported that 4 mg is more desirable than 2 mg, 2 mg is considered to be a suitable standard dose for rhinitis, as well 2 mg is a standard dose for asthma in Japan (Kumagai et al., 1982).

## CONCLUSION

As a result of the comparative study of HC and CF concerning efficacy, safety and usefulness using a double-blind method in several clinics, we can conclude that HC is superior to CF in efficacy and usefulness.

Irrespective of the patients background and the severity of symptoms, a higher improvement rate was obtained by administration of HC 1 mg × 2. Side-effects were mild and the frequency was similar to CF. Even though the rate of efficacy for HC increased in accordance with the length of administration, the lasting effect after discontinuation of the administration was not longer than the effect of CF. Different from CF, HC showed efficacy also in nasal obstruction.

## ZUSAMMENFASSUNG

In einer multizentrischen Doppelblindstudie verglichen wir Ketotifen (HC) und Clemastine-Fumarat (CF) in Bezug auf klinische Wirksamkeit, Nebenwirkungen, Labordaten und globale Beurteilung (durch Prüfer und Patienten) in 260 Patienten mit chronischer Rhinitis. HC wurde in zwei Dosierungen (0,5 mg und 1 mg zweimal täglich) und CF zweimal 1,34 mg/Tag verabreicht. Zu jeder Aktivsubstanz wurden die Placebos der beiden anderen während 4 Wochen mitverabreicht. Die Ergebnisse zeigen, dass HC 1 mg 2 × pro Tag der Dosierung von 0,5 mg 2 × pro Tag überlegen ist und letztere war immer noch wirksamer als CF in bezug auf Wirksamkeit und in der globalen Beurteilung. Die Nebenwirkungen beider HC-Dosierungen waren selten und sind mit denjenigen von CF vergleichbar. Im Gegensatz zu CF war HC in beiden Dosierungen in Fällen mit nasaler Obstruktion wirksam, wogegen CF und beide HC-Dosierungen in Bezug auf Niesen und Nasenfluss wirksam waren.

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