# Acrivastine versus Hydroxyzine in the Treatment of Cholinergic Urticaria

## *A Placebo-controlled Study*

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Kobza Black A, Aboobaker J, Gibson JR, Harvey SG, Marks P. Acrivastine versus hydroxyzine in the treatment of cholinergic urticaria. A placebo-controlled study. Acta Derm Venereol (Stockh) 1988; 68: 541–544.

Ten patients with cholinergic urticaria (CU) were entered into a double-blind, placebo-controlled, cross-over study. They were scheduled to receive acrivastine 8 mg t.d.s., hydroxyzine hydrochloride 20 mg t.d.s. and placebo according to a fully randomized, balanced treatment plan. Subjective clinical assessments and objective measurements following exercise challenge were performed during the study period. Both acrivastine and hydroxyzine were shown to be effective and well tolerated in the treatment of cholinergic urticaria. In addition, a trend was demonstrated for both active agents to improve peak expiratory flow rate (PEFR) following exercise, when compared with placebo, and this trend reached statistical significance in the case of acrivastine ($p<0.05$). *Key words: Exercise; Peak expiratory flow rate.* (Received April 5, 1988.)

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Cholinergic urticaria (CU) is characterized by distinctive, small, pruritic monomorphic weals surrounded by a red flare. The reaction develops in response to a rise in body core temperature, exercise, or emotional stress. $H_1$ antihistamines are generally considered to be partially effective in the management of CU and represent the mainstay of therapy. Hydroxyzine hydrochloride is one of the more commonly used agents in this therapeutic class. Acrivastine, a new, potent $H_1$ antihistamine, is a derivative of triprolidine with a low sedative profile (1) and negligible anticholinergic effects. It has previously been shown to be effective in the treatment of chronic idiopathic urticaria (2, 3) and idiopathic acquired cold urticaria (4).

We felt it to be of clinical interest to compare the effects of acrivastine and hydroxyzine hydrochloride in the management of CU, using both subjective clinical assessments during the full dosing period, and objective plus subjective measurements following exercise challenge. In addition, the effect of these agents on peak expiratory flow rate (PEFR) after exercise was evaluated.

## MATERIALS AND METHODS

### *Patients*

Ten patients (6 male, 4 female, mean age 30.3 years, range 19–67 years) with a clinical diagnosis of CU and a positive exercise challenge test were evaluated. The mean duration of CU was 8.6 years (range 3–20 years). The severity of CU on entry into the study was classified as mild in 6, moderate in 3 and severe in 1 patient.

*Treatment and clinical evaluation*

Trial materials were provided by The Wellcome Foundation Limited, London and consisted of acrivastine 8 mg (Semprex, Wellcome), hydroxyzine hydrochloride 20 mg (Atarax, Pfizer) and placebo presented in identical-looking capsules. Medications were allocated according to a fully randomized, double-blind, cross-over plan. Each treatment was taken three times per day for 5 days, with a 3-day break without medication for CU prior to commencing the study and a 2-day break between treatments. The taking of other medications, relevant to the treatment of CU or likely to cause sedation, was not permitted during the study period.

Treatment effects were documented using a detailed patient self-assessment form that was completed daily and an investigator's questionnaire. Data concerning efficacy, patient acceptability, adverse events and compliance with treatment were collected.

*The exercise challenge test*

This test was performed on entry into the study (baseline reading) and on day 5 of each treatment course 2 h after the patient had taken the last dose of the appropriate capsule. On each occasion, the patient exercised for 10 min on an exercise bicycle at a standardized pressure setting. Ten minutes after completing the exercise period a lesion count was performed over a pre-determined 400-$cm^2$ area on the patient's back. In addition, an overall assessment of the 'degree of reaction' was made by the investigator, patients completed a visual analogue scale relating to itching and PEFR was measured using a Wright's peak flow meter.

*Statistical analysis*

A professional medical statistician used the following methods for analysis of data, as appropriate: Sign test, analysis of variance and Newman-Keuls multiple range test.

## RESULTS

Results relating to the effects of the test agents following exercise challenge and during the full dosing periods are summarized in Tables I and II respectively. In all instances, efficacy trends favoured the active agents over placebo and on several occasions these trends reached statistical significance. No significant differences were demonstrated between the two active agents.

Table I. *Summary of exercise challenge test results*

| | Mean scores | | | |
|---|---|---|---|---|
| | Baseline | Placebo | Acrivastine | Hydroxyzine |
| Lesion count (square root) | 7.00 ($n$=10) | 5.80 ($n$=9) | 2.84* ($n$=10) | 3.20* ($n$=10) |
| Overall degree of reaction (investigators' assessment) (0=none, 4=severe) | 3.10 ($n$=10) | 2.56 ($n$=9) | 1.55 ($n$=10) | 2.02 ($n$=10) |
| Visual analogue scale (patients' assessment) (0=no itching, 100= very severe itching) | 55.7 ($n$=10) | 52.3 ($n$=9) | 29.7 ($n$=10) | 27.4 ($n$=10) |
| Peak expiratory flow rate (litres per minute) | 368.9 ($n$=9) | 397.9 ($n$=8) | 445.6* ($n$=8) | 410.2 ($n$=5) |

* Significantly different from placebo at the 5% level (Newman-Keuls multiple range test).

Reports of adverse events were few in number and evenly distributed between the three treatment groups. In particular, there was only one report of drowsiness in each treatment group during the study period.

## DISCUSSION

Current management of CU is not entirely satisfactory and the main therapeutic option involves the use of $H_1$ antihistamines. In view of variability in patient response and differences in the pharmacological profile of individual agents, it is desirable to have a range of alternative antihistamines. The availability of both traditional, sedating, and new generation low sedative profile antihistamines, permits the clinician to tailor the therapeutic regimen more precisely to individual patient needs. It is clearly worthwhile to establish the absolute and relative merits of individual antihistamines in specific dermatological conditions in which histamine is suspected of playing a pathogenetic role. CU is an appropriate and useful condition to study in this context as it is a relatively common form of the physical urticarias and lends itself to both subjective and objective evaluation. It is appreciated that the number of patients studied is small, but the data presented here indicate that both active agents are of benefit in the management of CU. Interestingly, the more objective aspects of the exercise challenge test produced trends in favour of acrivastine, whilst the more subjective data, derived both from the exercise challenge test and the clinical measurements during the full dosing periods, tended to favour hydroxyzine. In no case did such trends achieve statistical significance.

In view of the known association of an increase in bronchial reactivity in some patients with CU (5, 6), we felt it to be of interest to evaluate the effects of acrivastine and hydroxyzine on PEFR following exercise challenge. Both agents produced trends indicating positive effects on this parameter, with acrivastine yielding a statistically significant result ($p<0.05$, Newman-Keuls multiple range test). These data are consistent with a

Table II. *Summary of investigators' and patients' assessment of treatment effects*

| | Placebo | Acrivastine | Hydroxyzine |
|---|---|---|---|
| *Investigators' assessment (n=9)* | | | |
| Percentage of patients in whom the medication: | | | |
| Helped itching | 11 | 56 | 89* |
| Helped wealing | 22 | 89* | 89* |
| Helped itching most | 11 | 33 | 67 |
| Helped wealing most | 11 | 44 | 56 |
| Suited patient best overall | 11 | 44 | 56 |
| *Patients' self-assessment* | (n=9) | (n=10) | (n=10) |
| Percentage of patients in whom the medication: | | | |
| Helped | 56 | 80 | 100 |
| Mean scores (min=0, max=4) for: | | | |
| Degree of itching | 2.40 | 1.60** | 1.43** |
| Number of weals | 2.21 | 1.98 | 1.82 |
| Overall discomfort | 2.35 | 1.63* | 1.69* |
| Degree of improvement (min=0, max=3) | 0.74 | 1.24 | 1.58* |

* Significantly different from placebo at the 5% level (Newman-Keuls multiple range test).
** Significantly different from placebo at the 1% level (Newman-Keuls multiple range test).

previous suggestion (7) that potent antihistamines, when given in doses and/or routes of administration which permit high concentration in relevant tissues, can exert positive effects on parameters relevant to bronchial constriction in some patients with exercise-induced asthma.

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