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Initiation of the Effects of Acrivastine and Cetirizine on Histamine-induced Wheals and Itch in Human Skin

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The initiation of the antihistamine effect of a single dose of acrivastine (8 mg) or cetirizine (10 mg) on wheals and itch induced by histamine dihydrochloride (10 mg/ml) in the prick test was studied in a randomized cross-over design employing 20 healthy medical students. The prick test was performed before ingestion of the drug and after 15, 20, 25, 30, 60 and 90 min and 2, 3 and 4 h. Local symptoms (itching) were recorded on a visual analogue scale. The inhibitory effect of acrivastine on the histamine wheal was first noticed 20 min ($p < 0.01$) after ingestion of the drug and that of cetirizine after 60 min ($p < 0.001$). The maximum effect of cetirizine, at 4 h, was greater than that of acrivastine, at 3 h ($p < 0.001$). The suppression of itching was first noticed 25 min after ingestion with both drugs.

Key words: Prick testing; Histamine H_1-antagonists.

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The time of onset of the action of two new, non-sedative antihistamine drugs, acrivastine (1) and cetirizine (2), in suppressing the histamine-induced wheal and itch reaction in the human prick test was evaluated after a single peroral dose. The two drugs have not been compared earlier in this respect.

MATERIAL AND METHODS

The volunteer test subjects were 20 healthy medical students (13 females and 7 males, mean age 27 years). Each subject received first either acrivastine 8 mg (Semprex®, Wellcome Foundation Ltd. London, UK) or cetirizine 10 mg (Zyrtec®, UCB S.A., Brussels, Belgium) according to a randomization code, a second test being performed with the other drug after a wash-out period of at least 72 h. The medication was given by a trained nurse between 8.00 and 10.00 a.m., following a fasting period from midnight onwards. The tablets (ordinary commercial preparations) were prepacked in non-transparent plastic containers which were coded A or B, one dose in each container. The test subject or the nurse could not see the tablet and the test subject was asked to swallow it quickly with a glass of water.

Histamine dihydrochloride (Sigma Chemical Co., St. Louis, Mo., USA; 10 mg/ml in physiological NaCl) was used in the skin prick test performed on the volar forearm, the right and left forearm being used alternately. A histamine prick test was performed before administration of the antihistamine drug and after 15, 20, 25, 30, 60 and 90 min and 2, 3 and 4 h, by the same experienced person throughout, using the DHS prick lancet (Dome/Hollister-Stier, UK) which punctures the skin through a droplet of histamine solution, in a standardized manner. The size of the wheal was measured 10 min later and expressed as the mean of the maximum diameter and the maximum diameter perpendicular to it. Each test site was used only once. At the same time the subject was questioned about the severity of itching or other sensations at the test site, and the observations were marked on a 100 mm visual analogue scale.

The results were analysed statistically using the *t*-test for paired observations.

RESULTS

The beginning of the decrease in the size of the histamine wheal was noticed 20 min after the acrivastine dose ($p < 0.01$) (Fig. 1A), and the maximum effect was reached after 3 h. The subjective feelings of itching or tingling had decreased significantly 25 min after ingestion of the drug ($p < 0.05$) (Fig. 1B).

Cetirizine caused a significant decrease in the histamine wheal after 60 min ($p < 0.001$) (Fig. 1A), and its maximum antihistamine effect was reached at 4 h (the last observation time). The subjective feelings at the test site had decreased by 25 min after taking the drug ($p = 0.05$) (Fig. 1B).

The maximum antihistamine effect of cetirizine (at 4 h) was greater than the effect of acrivastine (at 3 h) ($p < 0.001$) (Fig. 1A).

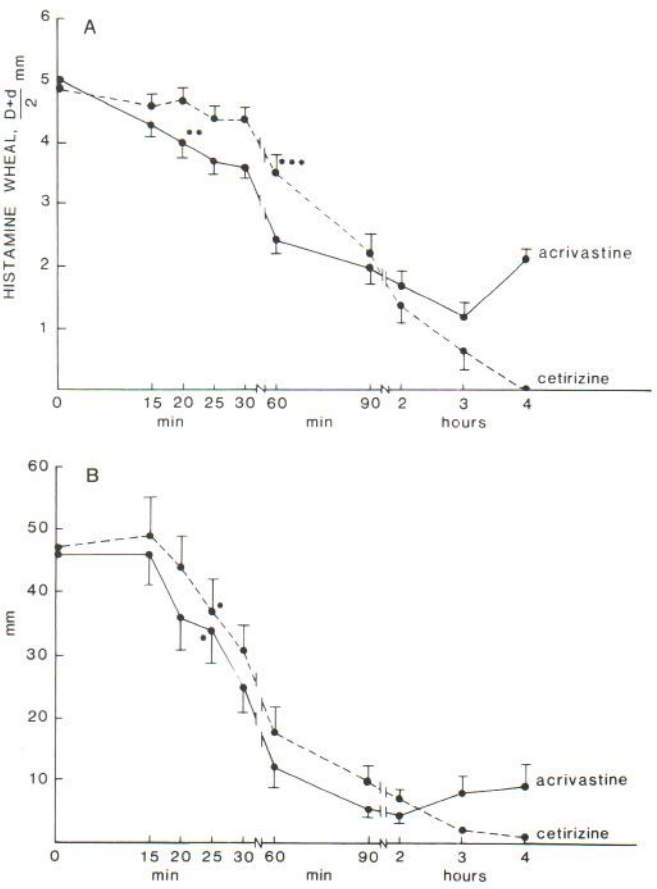

Fig. 1. Effect of a single peroral dose of acrivastine (8 mg) or cetirizine (10 mg) on wheals (A) and local itching (B) induced by histamine dihydrochloride (10 mg/ml) in the prick test on the volar forearms of 20 test subjects. Mean and SEM, $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

DISCUSSION

In a previous test with intradermally injected histamine, the antihistamine effect of acrivastine was observed 30 min after intake, which was also the first point of time at which the effect was evaluated (3). The peak effect was then reported to occur 2 h after intake. The present trial produced an antihistamine effect 10 min earlier (at 20 min), and peak inhibition occurred after 3 h, although there was no statistical difference between the wheal sizes at 2 and 3 h (Fig. 1A).

The initiation of the inhibitory effect of 10 mg cetirizine on histamine-induced wheals has been reported to appear as early as at 20 min after peroral intake (4), or, in another test, at 40 min or 60 min depending on whether the wheal size was compared with a placebo or baseline standard (5). Supporting the results of the latter evaluation, we first noticed an antihistamine effect after 60 min. It is not known why the histamine itch was relieved after only 25 min following cetirizine intake, whereas the decrease in the histamine wheal was not noticed until at 60 min.

Both acrivastine and cetirizine are quick-acting drugs after peroral intake and are suitable for "on-demand" medication.

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